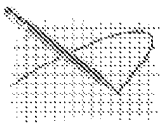
EXHIBIT 10



Pierre V Tran /AM/LLY
11/11/2002 08:44 PM

To Walter Deberdt/AM/LLY@Lilly
cc David G Perahia/EMA/LLY@Lilly, Dick Veldhuis/EMA/LLY@Lilly, Ilker Yalcin/AM/LLY@Lilly, John H April/AM/LLY@Lilly, Lily Zahed/AM/LLY@Lilly, Michael Detke/AM/LLY@Lilly, Richard Bump/AM/LLY@Lilly
bcc
Subject Re: comments on SUI clinical expert report

Walter,
Thanks for taking the time to review the SUI CER and offer your valuable comments.
Pierre
Walter Deberdt

Walter Deberdt
11/11/2002 06:44 PM

To: Richard Bump/AM/LLY@Lilly, Ilker Yalcin/AM/LLY@Lilly
cc: John H April/AM/LLY@Lilly, Michael Detke/AM/LLY@Lilly, David G Perahia/EMA/LLY@Lilly, Pierre V Tran/AM/LLY@Lilly, Dick Veldhuis/EMA/LLY@Lilly, Lily Zahed/AM/LLY@Lilly
Subject: comments on SUI clinical expert report

Richard, Ilker,

As you may know I'll work together with David and John on the MDD CER. So I read with much interest (during the rainy weekend) the SUI CER. I have written my comments in red in the attached document. I appreciated very much all the hard work that must have gone in this review and besides the few items that I'm listing here below I'm convinced you have made a very useful document which is nice to read (when it's raining outside).

I read through this document in a 'naive' condition: I don't know much about SUI and I just started working on duloxetine. I thought this could be useful for you since CPMP members don't know much about SUI and duloxetine neither. I also took the approach that the CER should be readible as a stand alone document, because the CPMP members may not want to look up numbers and % in the Summaries or in the Study Reports.

As you can see in my comments in the CER, I fear that the pharmacokinetics section in the actual wording shows too much doubt and uncertainty.

In the efficacy section one should pay attention to the difference between SBAT in I-QOL compared to the other studies, and the possible explanations for this difference, since this is the European phase III study. CPMP is likely to be sensitive on this.

Knowing a bit the CPMP sensitivity for maintenance of effect and relapse rates, I'd add some discussion on these.

I think it is important to discuss the early discontinuations due to AE in relationship to uptitration like in SAAW, compared to the other studies; especially if these early DC/AEs were making the difference between the 'European' SBAT study and the other studies.

Discontinuation symptoms are a big deal in MDD (thanks to ourselves with Prozac promotion). **Mike**, can you confirm that for MDD we would propose a gradual tapering? It would seem logic that if we propose this for MDD, we would recommend it also for SUI.

Finally, I'd be glad to discuss these and other topics in more detail with you. I'm sure I would learn from such a discussion. So, if you hav e some time for this, please send me an invitation when it is convenient for you. **Many thanks,**

Walter Deberdt
Sr. Clinical Research Physician

tel +1 317 651 5329
cell +1 317 985 7009

EXHIBIT 11

David G Perahia /EMA/LLY
07/02/2003 11:36 AM

To Madelaine M Wohlreich/AM/LLY@Lilly
cc John M Plewes/AM/LLY@Lilly, Melissa J Joliat/AM/LLY@Lilly, Michael Detke/AM/LLY@Lilly, Nancy Jean Trapp/AM/LLY@Lilly
bcc David G Perahia/EMA/LLY
Subject Re: An obscure question

Cheers, Madelaine - you've hit the nail squarely on the head !

It's not that the discontinuation issue will necessarily be something we can proactively use to sell duloxetine (I believe not, at least from a historical perspective), more that it's something that the media and regulatory authorities might well latch on to unless we are proactive about it. I sense we are being a bit complacent around this, and it could hurt us (e.g. no diffs from parox on abrupt discontinuation in our trials, short t1/2 etc. etc.)

As an opening gambit, I would define proactive as :

(1) Write up our data and get it published as a priority rather than dragging our heels
(2) Consider running a trial which might add to the evidence base on how best to manage stopping the drug, e.g. over how long should drug be tapered ? (open label treatment, then perhaps 3 arms looking at abrupt discontinuation vs. 2 week taper vs. 4 week taper in a double blind fashion, with frequent visits). Good PR due to being open and pushing the science, with an evidence-based recommendation at the end to boot. I'm sure Matt would blanch at this suggestion, but we can't just stick our head into the sand.

Paroxetine is being torn to pieces by the media (and in fact regulators too) over in Europe, and much of the criticism is stemming from the perception that GSK have been, to put it politely, less than transparent about discontinuation with paroxetine and how best to manage it. I would rather we didn't fall into the same trap.

Re : writing resource, I can look into this. I'm certainly willing to offer my services as an author on a manuscript discussing discontinuation with duloxetine, however, and there is the perfect thought leader in the UK (Peter Haddad, who has published pretty widely on the topic in general) to work on it with us.

D.

Madelaine M Wohlreich

Madelaine M Wohlreich
02/07/2003 16:01

To: Michael Detke/AM/LLY@Lilly
cc: David G Perahia/EMA/LLY@Lilly, John M Plewes/AM/LLY@Lilly, Melissa J Joliat/AM/LLY@Lilly, Nancy Jean Trapp/AM/LLY@Lilly
Subject: Re: An obscure question

The feeling here has been that since it will be in our FDA label that tapering is recommended, that there is not a lot more that needs to be done proactively.
When we have said at consulting conferences that discontinuation type side effects could be seen on abrupt taper, clinicians have not appeared to be terribly concerned.

Madelaine
Michael Detke

Michael Detke
07/02/2003 09:47 AM

To: David G Perahia/EMA/LLY@Lilly
cc: Melissa J Joliat/AM/LLY@Lilly, John M Plewes/AM/LLY@Lilly, Nancy Jean Trapp/AM/LLY@Lilly, Madelaine M Wohlreich/AM/LLY@Lilly

Subject: Re: An obscure question

David:

Redacted

Is there any possibility of writing resources in the region/country?

-Mike

Michael J. Detke, M.D., Ph.D.
Lilly Research Laboratories
Lilly Corporate Center
Indianapolis, IN 46285
(317) 277-6420
(317) 276-6026 - fax
mdetke@lilly.com

David G Perahia

David G Perahia
07/02/2003 02:46 AM

To: Michael Detke/AM/LLY@Lilly
cc:
Subject: Re: An obscure question

OK Miguel.

I must confess to being a little unconfortable about the whole discontinuation thing. Maybe it's more of a UK specific issue, but paroxetine is taking a fearsome battering in the media over here at the moment, and a significant part of that is discontinuation-related stuff. It's clear that duloxetine has a significant DESS liability (on abrupt discontinuation, admittedly, but how much taper data do we have yet ?), and the perception will be further reinforced by our short t1/2 which is seen by many as being directly linked (Redacted Redacted

I've already asked Melissa to look into what publications we have on our "to do" list in this area. If we're not careful, the environment is set for this to blow up in our faces unless we're proactive about it.

Diego.

Michael Detke

Michael Detke
01/07/2003 19:43

To: David G Perahia/EMA/LLY@Lilly
cc:
Subject: Re: An obscure question

David, I think most of the studies checked at one week, and we probably don't have the data broken out in finer temporal intervals than that.

Sorry amigo,

-Miguel

Michael J. Detke, M.D., Ph.D.
Lilly Research Laboratories
Lilly Corporate Center
Indianapolis, IN 46285
(317) 277-6420
(317) 276-6026 - fax
mdetke@lilly.com

David G Perahia

David G Perahia
06/30/2003 11:13 AM

To: Michael Detke/AM/LLY@Lilly
cc:
Subject: An obscure question

Hi hombre,

Quick question : I was recently asked whether we have any discontinuation data at around 3 days post-discontinuation, this being the time when you might expect maximal symtomatology (approx. 5 half-lives after the final dose). I didn't think we did, but thought I'd check.

Cheers,

David.

EXHIBIT 12

David G Perahia /EMA/LLY
07/02/2003 11:36 AM

To Madelaine M Wohlreich/AM/LLY@Lilly
cc John M Plewes/AM/LLY@Lilly, Melissa J Joliat/AM/LLY@Lilly, Michael Detke/AM/LLY@Lilly, Nancy Jean Trapp/AM/LLY@Lilly
bcc David G Perahia/EMA/LLY
Subject Re: An obscure question

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02/07/2003 16:01

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cc: David G Perahia/EMA/LLY@Lilly, John M Plewes/AM/LLY@Lilly, Melissa J Joliat/AM/LLY@Lilly, Nancy Jean Trapp/AM/LLY@Lilly
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Michael Detke
07/02/2003 09:47 AM

To: David G Perahia/EMA/LLY@Lilly
cc: Melissa J Joliat/AM/LLY@Lilly, John M Plewes/AM/LLY@Lilly, Nancy Jean Trapp/AM/LLY@Lilly, Madelaine M Wohlreich/AM/LLY@Lilly

Subject: Re: An obscure question

David:

I think it is somewhat geography-specific, but I'm not entirely sure how much. I was told by someone who was then a Prozac sales rep in the US that they tried to increase the importance of DESS and half-life in prescribing decisions, as it was rated as the 30th most important on a list of 30 issues by prescribers, and after concerted education about the issue, it moved all the way up to about 28th. But that was a while ago. I'll let Madelaine or John comment further.

Is there any possibility of writing resources in the region/country?

-Mike

Michael J. Detke, M.D., Ph.D.
Lilly Research Laboratories
Lilly Corporate Center
Indianapolis, IN 46285
(317) 277-6420
(317) 276-6026 - fax
mdetke@lilly.com

David G Perahia

David G Perahia
07/02/2003 02:46 AM

To: Michael Detke/AM/LLY@Lilly
cc:
Subject: Re: An obscure question

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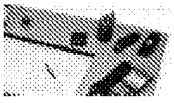
I've already asked Melissa to look into what publications we have on our "to do" list in this area. If we're not careful, the environment is set for this to blow up in our faces unless we're proactive about it.

Diego.

Michael Detke



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Sorry amigo,

-Miguel

Michael J. Detke, M.D., Ph.D.
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David G Perahia

David G Perahia
06/30/2003 11:13 AM

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cc:
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Cheers,

David.

EXHIBIT 13

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF VIRGINIA
ALEXANDRIA DIVISION

JANINE ALI, Plaintiff, v. ELI LILLY AND COMPANY, an Indiana corporation, Defendant.	Case No. 1:14-cv-01615-AJT-JFA Hon. Anthony J. Trenga Hon. John F. Anderson **PLAINTIFF'S SECOND SET OF REQUESTS FOR PRODUCTION**
GILDA HAGAN-BROWN, Plaintiff, v. ELI LILLY AND COMPANY, an Indiana corporation, Defendant.	Case No. 1:14-cv-01614-AJT-JFA Hon. Anthony J. Trenga Hon. John F. Anderson **PLAINTIFF'S SECOND SET OF REQUESTS FOR PRODUCTION**

PLAINTIFF'S SECOND SET OF REQUESTS FOR PRODUCTION

Propounding Party: Plaintiffs Janine Ali and Gilda Hagan-Brown

Responding Party: Defendant Eli Lilly and Company

Set Number: Two (2)

Plaintiffs Janine Ali and Gilda Hagan-Brown, by and through their attorneys, and pursuant to Federal Rule of Civil Procedure 26 and 34, do hereby serve written request upon Defendant Eli Lilly and Company ("Lilly") to produce for inspection and reproduction the following documents and things specified below at the offices of Baum, Hedlund, Aristei & Goldman, P.C., 12100 Wilshire Boulevard, Suite 950, Los Angeles, CA 90025, in accordance

with the following definitions and instructions and within thirty (30) days of service.

DEFINITIONS

The following definitions apply to each request below and are incorporated therein:

1. "ALL" means "any and all" and the word "any" means "any and all."

2. The term "CYMBALTA" means duloxetine hydrochloride, including any other name or trademark under which it is sold, domestically *or* abroad, marketed or produced, including products sold, marketed, or produced by others if they do so with your permission, at your request, at your direction, with your acquiescence, and/or if you gain any benefit from their sales, marketing, or distribution.

3. The term "COMMUNICATION" means and refers to every method and manner of transmitting or receiving data, opinions, thoughts, inquiries, representations and other information, whether orally, in writing, electronically, or otherwise, between two or more persons or entities. Communications include drafts and other written information intended for communicating to another person, even if not ultimately transmitted to or received by another person.

4. The terms "CONCERNING," "RELATING," and/or "REGARDING" mean containing, alluding to, responding to, commenting upon, discussing, explaining, mentioning, analyzing, constituting, memorializing, comprising, repeating, incorporating, confirming, listing, evidencing, setting forth, summarizing, or characterizing, either directly or indirectly, in whole or in part.

5. The term "DEAE" means Discontinuation Emergent Adverse Event, and refers to any possible side effects or symptoms relating to discontinuing, withdrawing, or tapering from the use, consumption, or treatment with Cymbalta.

6. The term "WITHDRAWAL" includes discontinuation or tapering, as well as DEAEs, withdrawal symptoms, and any side effects of withdrawing, discontinuing, or tapering from CYMBALTA.

7. The term "DOCUMENT" shall have the broadest meaning possible under Rule 34 of the Federal Rules of Civil Procedure and includes all originals and drafts, in any and all languages, of any nature whatsoever, in your possession, custody or control, regardless of where located, and include, but are not limited to, letters, correspondence, logs, drafts, contracts, prospective contracts, agreements, reports, records, studies, surveys, resolutions, tabulations, notes, summaries, memoranda, Electronically Stored Information ("ESI"), electronic mail ("email"), calendar or diary entries, handwritten notes, working papers, work sheets, spread sheets, diagrams, minutes of meetings, agendas, bulletins, periodicals, circulars, advertisements, notices, announcements, invoices, statements, checks (front and back), bank statements, ledgers, orders, vouchers, instructions, drawings, charts, graphs, manuals, brochures, pamphlets, schedules, telegrams, teletypes, photographs, audio tapes, voice-mail messages, videotapes, electronic recordings, facsimile transmissions, and information of whatever kind either stored on computers, including computer disks, hard drives and other media, or contained in any computer or information retrieval devices.

8. The terms "ELI LILLY," "LILLY," "YOU" or "YOUR" refer to Eli LILLY and Company, its respective officers, directors, employees, representatives, subsidiaries, and affiliates thereof, as well as all persons acting for, on behalf of, or in concert with Eli LILLY and Company's behalf, including agents, attorneys, accountants, and investigators.

9. The term "FDA" means the United States Food & Drug Administration.

10. The term "INCLUDING" means "including, but not limited to."

11. The term "LABEL" refers to the official prescribing information for the drug, including but not limited to the product insert and medication guides approved by the FDA or other foreign regulatory bodies.

12. The term "MEDICAL PROFESSIONAL" includes healthcare providers, prescribing doctors, non-prescribing doctors, physicians, pharmacists, nurses, and other individuals who provide healthcare services.

13. The term "PERAHIA ARTICLE" refers to David G. Perahia, *et al.*, *Symptoms Following Abrupt Discontinuation of Duloxetine Treatment in Patients with Major Depressive Disorder*, 89 J. Affective Disorders 207-12 (2005).

14. The term "SNRI" means serotonin norepinehprine reuptake inhibitor.

15. The term "SSRI" means selective serotonin reuptake inhibitor.

16. The use of the terms "or," "and," and "and/or" should be construed conjunctively and disjunctively for the broadest possible meaning.

17. The term "person" or "people" includes individuals, corporations, partnerships, associations, and other bodies and entities, as well as their representatives, agents, employees and attorneys.

18. The terms "research," "study," or "analysis," when used as a noun mean and refer to any research, analysis, study, report, evaluation or assessment. The term research when used as a verb means to research, analyze, study, report, evaluate, or assess.

19. The term "use" means to "employ something for a purpose," "to do something habitually," "to consume something," "to manipulate," "to benefit from," as well as to allow others to "use," or acquiesce in others' "use."

20. The singular use of any term or phrase includes its plural, and the plural of any term or phrase includes its singular.

21. The use of any tense of any verb shall also include within its meaning all other tenses of that verb.

INSTRUCTIONS

1. You must serve your responses and any objections within 30 days after being served the requests.

2. Each paragraph and subparagraph of each request should be construed independently, and not be referenced to any other paragraph or subparagraph of this request for purposes of limitation.

3. Pursuant to the Fed. R. Civ. P. 26(e), these requests are continuing in nature, so as to require a supplemental response to correct any incomplete or incorrect answer based on information you may become aware of between the time of your initial response and the time of trial.

4. In responding to these requests, you shall respond based on information in your possession, custody, or control, including (by way of illustration only and not limited to) information in the possession, custody, or control of your affiliates, subsidiaries, or subcontractors, your present or former attorneys, accountants, directors, officers, partners, employees, other representatives and agents, independent contractors over which or whom you have or have had control, and any other persons acting on your behalf.

5. Notwithstanding the assertion of any objection to production, any documents as to which an objection is raised that also contain non-objectionable matter that is relevant and material to a request herein must be produced, but that portion of the documents for which the

objection is asserted may be redacted, provided that the material redacted is listed in the privilege log.

6. If you claim that the attorney-client privilege, or any other privilege, doctrine or reason for withholding a document is applicable, please set forth in writing and with your response to this Request: (1) the date of the document; (2) the type of document; (3) the subject matter of the document; (4) the name, employment and title of each person who prepared or received the document or any copy thereof; and (5) the basis for the claim of privilege or other ground for withholding the document. If you claim only part of the document is privileged or otherwise need not be produced, please produce the remaining part of the document. In the case of attorney work-product privilege, you must also identify the litigation for which the work-product was prepared.

7. If any document to be produced has been lost, discarded, transferred to another person or entity, destroyed, or otherwise disposed of, please set forth in writing: (1) the date, name and subject matter of the document; (2) the name, employment and title of each person who prepared, received, reviewed, or had custody, possession, or control of the document; (3) all persons with knowledge of the contents or any portion of the contents of the document; (4) the previous location of the document; (5) the date of disposal or transfer of the document; (6) the reason for disposal or transfer of the document; and, if applicable, (7) the manner of disposal of the document; or, if applicable, (8) the names and addresses of the transferees of the document.

8. For the convenience of the Court and the parties, Plaintiffs request that each request be quoted in full immediately preceding the answer.

9. Whenever a reference to a business entity appears, the reference shall mean the business entity, its affiliated entities, partnerships, divisions, subdivisions, directors, officers, employees, agents, clients, or other representatives of affiliated third parties.

10. Unless specified by the request, there is no time limitation to any of these requests.

11. As provided by Federal Rule of Civil Procedure Rule 34(b)(2)(E)(iii), please produce all electronically stored information in their native electronic format with all metadata preserved in a *.DAT file format. "Electronically stored information" includes the full scope of that term as contemplated by Federal Rule of Civil Procedure Rule 34, and refers to all computer or electronically stored or generated data and information, and shall include all attachments to the enclosures with any requested item, to which they are attached or with which they are enclosed, and all drafts thereof. "Electronically stored information" includes, but is not limited to, all information stored in any format on any storage media, including for example, but not limited to: hard disks, floppy disks, optical disks, flash memory devices, and magnetic tape, whether fixed, portable, or removable. The format of "electronically stored information" includes, for example, but is not limited to: word processing documents, electronic spreadsheets, electronic presentation documents, email messages, image files, sound files, material or information stored in a database, or accessible from a database, of whatever description. "Electronically stored information" also includes all associated metadata that is routinely maintained or saved, which includes for example, but is not limited to document title or name, file name, date and time of creation, date and time of last edit, identity of author, identity of owner, identities of editors, identities of recipients, changes, history of changes, email header information, and email routing information.) Please produce all metadata in a *.DAT file format.

If a document contains a single redaction, please provide the appropriate metadata for the remainder of the document, notwithstanding the redactions and the information provided separately as part of a privilege log.

12. For the convenience of the parties and to reduce production costs, please produce all DOCUMENTS which exist only in hardcopy, i.e., cannot be produced in the electronic format discussed above, form in an electronic format such as a *.PDF format or equivalent.

13. In response to each request, please specifically reference which Bates numbered pages are responsive to *that* request. Generalized reference to categories of documents is the equivalent of no response at all. If no DOCUMENTS are responsive, please indicate such. If you are not responding to a request or any portion therein, please indicate such.gh

REQUESTS FOR PRODUCTION

2ND SET, RFP NO. 1: Please produce the results, summaries, and/or presentations concerning market surveys and/or focus groups for PROZAC that mention, measure, or refer to WITHDRAWAL or discontinuation symptoms.

2ND SET, RFP NO. 2: Please produce all marketing plans, market analyses, pricing studies, patient segmentation studies, conjoint studies / discrete choice studies, and/or any form of marketing evaluation of PROZAC that mention or discuss the issue of WITHDRAWAL or discontinuation symptoms.

2ND SET, RFP NO. 3: Please produce all marketing and/or sales documents that discuss, mention, or compare the WITHDRAWAL profile of Prozac to other antidepressants, including but not limited to CYMBALTA, Zoloft, Effexor, Paxil, Celexa, and Lexapro.

2ND SET, RFP NO. 4: Please produce all DOCUMENTS reflecting the amount of compensation, including but not limited to direct payments and stock options, given to the

following current and/or former Lilly employees: Michael Detke, David Perahia, Sharon Hoog, Steven Knowles, Sara Mescher, Nayan Acharya, Mark Bangs, Greg Brophy, Bryan Boggs, Anne Sakai-Robbins, John Hixon, Antonio Crucitti, Madeleine Wohlreich, Matt Kuntz, Isabelle Murray, Torkil Fredborg, and Carol Stephens.

DATED: April 15, 2015

Respectfully submitted,

MILLER LEGAL

/s/ Peter A. Miller
Peter A. Miller, Esq.
Va. Bar 47822
pmiller@millerlegalllc.com
175 S. Pantops Drive, Ste. 301
Charlottesville, VA 22911
Tele (434) 529-6909
Fax (888) 830-1488

BAUM, HEDLUND, ARISTEI & GOLDMAN, P.C.
R. Brent Wisner, Esq. (*pro hac vice*)
rbwisner@baumhedlundlaw.com
12100 Wilshire Blvd., Suite 950
Los Angeles, CA 90025
Tel: (310) 207-3233
Fax: (310) 820-7444

Attorneys for Plaintiff

CERTIFICATE OF SERVICE

I hereby certify that on this 15th day of April, 2015, a true and correct copy of the foregoing PLAINTIFF'S SECOND SET OF REQUESTS FOR PRODUCTION was served via Electronic Mail, upon the following:

Michael X. Imbroscio
mimbroscio@cov.com
Phyllis A. Jones
pajones@cov.com
Jeffrey T. Bozman
jbozman@cov.com
Brian Stekloff
bstekloff@cov.com
COVINGTON & BURLING LLP
One City Center
850 Tenth Street, NW
Washington, DC 20001

Attorneys for Eli Lilly and Company

Samantha Jison

EXHIBIT 14

Wisner, R. Brent

From: Wisner, R. Brent
Sent: Wednesday, April 22, 2015 12:11 AM
To: 'Stekloff, Brian'
Cc: Esfandiari, Bijan; T. Matthew Leckman; Baum, Michael; Broomandan, Amber; pmiller@millerlegalllc.com; Imbroscio, Michael; Jones, Phyllis; Ullman, Emily; Reynolds, Brett; Mike Woerner
Subject: RE: Ali and Hagan-Brown: Pending Discovery Issues

Brian,

Before we delve into the issues below, I would like to formally request that Lilly agree to produce all privilege logs for the *Ali* and *Hagan-Brown* cases by no later than May 15, 2015 (the last day of discovery). The protective order allows a party to request an expedited privilege log provided there is good cause. Since Plaintiffs would like the ability to challenge any privilege determinations, if appropriate, before trial, I believe there is good cause to request a privilege log production by the final day of discovery.

Thanks for following up on these issues. I will address each in turn.

Matthew Kuntz

Provided you and Mr. Kuntz know that I will try my best to be at the deposition by 1:00 p.m. but may be late, I will notice the deposition for 1:00 p.m. and make my best effort to have us out of there by 6:00 p.m. I will get you the deposition notice tomorrow. I assume, based on our prior conversation, we will be getting Mr. Kuntz's emails by April 27, 2015.

Isabelle Murray

Much appreciated. Can you please advise when we can expect to receive these documents, as well as the emails for Ms. Stephens and Dr. Crucitti. As you know, timing is crucial in these cases.

Plaintiffs' Second Set of RFPs

As you know, Plaintiffs allege that Lilly promoted Prozac as being superior to other antidepressants because of its superior withdrawal profile. Plaintiffs allege that once Prozac went off patent, Lilly needed a new antidepressant blockbuster and thus focused its marketing on Cymbalta. The problem, however, was that Cymbalta was significantly more risky vis-à-vis withdrawal so, Plaintiffs' allege Lilly downplayed the risk. The first two Prozac requests seek documents wherein Lilly conducted marketing surveys, focus groups, segmentation studies, message testing, etc., and one of the issues mentioned or discussed was risk of discontinuation symptoms / withdrawal. To put this in context, Lilly produced several marketing studies and summaries about Cymbalta which showed that the risk of withdrawal was important to pricing and prescribing decisions. *See, e.g.*, CYM-02783656; CYM-02783711; CYM-02783884; CYM-02783967; CYM-02784114; CYM-02785859; CYM-02785914; and CYM-02786215. That production was not major—only about a 100 documents. We are looking for the same about

Prozac, but have limited the search to the issue of withdrawal—for Cymbalta we asked for all marketing documents. *See* RFP No. 80. For reference, these are two document requests I am referring to:

> **2ND SET, RFP NO. 1:** Please produce the results, summaries, and/or presentations concerning market surveys and/or focus groups for PROZAC that mention, measure, or refer to WITHDRAWAL or discontinuation symptoms.
>
> **2ND SET, RFP NO. 2:** Please produce all marketing plans, market analyses, pricing studies, patient segmentation studies, conjoint studies / discrete choice studies, and/or any form of marketing evaluation of PROZAC that mention or discuss the issue of WITHDRAWAL or discontinuation symptoms.

For 2ND Set, RFP No. 3, plaintiffs are looking for something slightly different, but also very focused. For reference, the request reads:

> **2ND SET, RFP NO. 3:** Please produce all marketing and/or sales documents that discuss, mention, or compare the WITHDRAWAL profile of Prozac to other antidepressants, including but not limited to CYMBALTA, Zoloft, Effexor, Paxil, Celexa, and Lexapro.

This request seeks (1) Prozac marketing plans that the discuss promotion of Prozac's superior withdrawal profile as way to position Prozac as being superior to competing antidepressants / increase sales/prescriptions, and (2) sales aids / "slim-jims" / brochures used by Lilly's sales reps to compare Prozac's withdrawal profile to other antidepressants. This does not contemplate a massive production (unless Lilly has extensive documentation on this).

I hope this clarifies the issue and prompts Lilly to produce these documents. The RFPs were served on April 15, 2015, so Lilly's objections are not due until May 1, 2015. It would be great if Lilly could get me its objections a little sooner, i.e., April 29, 2015, so I can get any needed motion to compel on file by May 1, 2015, for a hearing on May 8, 2015. We already know I plan to move on the salary issue, so it would be great to have these issue t-d up for resolution as soon as possible.

30(b)(6) regarding Clinical Trials

I think we may have had a bit of confusion on this. I plan to question this 30(b)(6) witness about ***all*** Cymbalta clinical trials, with a focus on issues of discontinuation symptoms, i.e., DEAEs, DESS, T(aper)EAEs, etc. I plan to show the witness every study report that had a measurement of discontinuation symptoms. In no way was this deposition going to be limited to the nine trials for abrupt discontinuation for MDD discussed in the Perahia article. I also plan to ask questions about any meta-analysis that may have been done, and if not, why it was not done. I plan to talk about what the studies show, i.e., whether there is a difference between abrupt v. taper, and examine how Cymbalta compared with other drugs such as Prozac and Paxil.

Dr. Fredborg/30(b)(6) regarding capsule design

Please let me know about Dr. Fredborg as soon as possible. I am hoping we can arrange for this deposition for May 6, 7, or 8. The latest would be May 11, 2015. Also, please let me know when we can expect the remaining emails for Dr. Fredborg, i.e., the ones from Lilly's European servers.

I will pencil in May 7, 2015 for the 30(b)(6) regarding the development and creation of the Cymbalta capsule and dosing, pending a ruling from the Court.

Access to Ice Miller

Michael Woerner and I will be attending the depositions on April 28-30.

Best,

Brent

From: Stekloff, Brian [mailto:BStekloff@cov.com]
Sent: Tuesday, April 21, 2015 8:53 AM
To: Wisner, R. Brent
Cc: Esfandiari, Bijan; T. Matthew Leckman; Baum, Michael; Broomandan, Amber; pmiller@millerlegalllc.com; Imbroscio, Michael; Jones, Phyllis; Ullman, Emily; Reynolds, Brett
Subject: Ali and Hagan-Brown: Pending Discovery Issues

Brent:

I write to follow-up on a few pending discovery issues in Ali and Hagan-Brown:

Matthew Kuntz

We can confirm his deposition for May 6. I understand that you would like to start at 2:00. Mr. Kuntz would prefer to start at 1:00 so he can be done by 6:00 at the latest. If you agree, please notice the deposition for 1:00. We understand that you have court that morning and that may cause you to be late. Mr. Kuntz resides in Libertyville, IL, which is north of Chicago. We have identified a hotel in Libertyville where we think it makes sense for the deposition to take place: http://doubletree3.hilton.com/en/hotels/illinois/doubletree-by-hilton-hotel-libertyville-mundelein-CHIMUDT/event/index.html. We contacted the hotel to check on space and there is availability on May 6. Our understanding is that the room will cost $350.00 for the day. If you agree to hold the deposition at this location, please contact the catering manager to reserve the space. Finally, assuming these logistics work for you, please send us a notice today, if possible.

Isabelle Murray

We will agree to produce her documents consistent with the understanding we have reached with respect to other witnesses, including Dr. Crucitti and Carol Stephens, *i.e.*, we only will review emails from the time period during which she worked on Cymbalta, i.e., during the 2012 time period. Please confirm your agreement.

Plaintiffs' Second Set of RFPs

Following court last week, you told us that your Prozac requests were limited and that you are only seeking approximately 50-60 documents. Please send us the description of the approximately 50-60 documents that you seek

so that we can prepare our responses/objections. As we discussed, we will object to the request related to employees' salaries.

30(b)(6) regarding Clinical Trials

Following court last week, we also discussed the topics you would like to cover during the 30(b)(6) deposition. Based on that discussion, we will have Dr. Wohlreich prepared on the following subject matter:

For each of the nine trials analyzed in Perahia, D.G. et al., *Symptoms following abrupt discontinuation of duloxetine treatment in patients with major depressive disorder*, 89 J. Affective Disorders 207 (2005) ("Perahia 2005"):

a. With respect to DEAEs, the methodology and any safety measures collected related to DEAEs.

b. Results related to DEAEs.

Please let us know if there are other topics that you would like to address at the deposition. Moreover, if you intend to ask questions about clinical trials other than the nine trials analyzed in Perahia 2005, please let us know by close of business on Monday, April 27 so that we can prepare Dr. Wohlreich accordingly.

Dr. Fredborg/30(b)(6) regarding capsule design

We are working on a date for Dr. Fredborg and I will keep you updated. Please reserve May 7 for the tentative deposition of a 30(b)(6) witness regarding capsule design in Indianapolis, subject to the Court's ruling on that issue.

Plaintiffs' RFA No. 29

We hope to be able to respond to you by the end of the week regarding our response.

Access to Ice Miller

For the depositions that will take place in Indianapolis next week, we need to provide Ice Miller with the names of attendees for security access to the building. Please send me the names of the attorneys that will be at the depositions on April 28-30.

Thanks,

Brian

Brian Stekloff

Covington & Burling LLP
One CityCenter, 850 Tenth Street, NW, Washington, DC 20001
T +1 202 662 5057 | bstekloff@cov.com
www.cov.com

COVINGTON

EXHIBIT 15

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF VIRGINIA
ALEXANDRIA DIVISION

JANINE ALI, Plaintiff, v. ELI LILLY AND COMPANY, an Indiana corporation, Defendant.	CASE NO.: 1:14-CV-01615-GBL-TRJ

DEFENDANT'S OBJECTIONS TO PLAINTIFF'S SECOND SET OF REQUESTS FOR PRODUCTION OF DOCUMENTS

Defendant Eli Lilly and Company ("Defendant" or "Lilly") hereby submits its objections to Plaintiff's Second Set of Requests for Production, as follows:

GENERAL STATEMENT AND OBJECTIONS

Lilly objects to these Requests as overly broad, unduly burdensome, and not in proportion to the needs of the case, particularly to the extent they seek documents or information that are already in Plaintiff's possession, custody, or control.

OBJECTIONS TO DEFINITIONS AND INSTRUCTIONS

1. Lilly objects to the definitions of the terms "ELI LILLY", "LILLY", "YOU", and "YOUR" to the extent that they seek to extend these definitions to persons or entities other than the named Defendant in this litigation, Eli Lilly and Company, and purport to call for information or documents that are not in the possession, custody, or control of Eli Lilly and Company. For purposes of its objections and responses, Lilly will define "ELI LILLY",

"LILLY", "YOU", and "YOUR" to mean Eli Lilly and Company. Lilly will limit its responses to information and documents that are in the possession, custody, or control of Eli Lilly and Company.

2. Lilly objects to the definition of "DOCUMENT" to the extent that it imposes obligations on Lilly beyond those in the Federal Rules of Civil Procedure.

3. Lilly objects to Instruction Number 1 to the extent that it does not comport with the Federal Rules of Civil Procedure and the Local Civil Rules of the Eastern District of Virginia.

4. Lilly objects to Instruction Number 7 to the extent that it imposes burdens on Lilly beyond its obligations under the Federal Rules of Civil Procedure.

5. Lilly objects to Instruction Number 11 to the extent that its use of the term "Electronically stored information" imposes burdens on Lilly beyond its obligations under the Federal Rules of Civil Procedure. Lilly also objects to the extent that this Instruction calls for the search and production of information from, including but not limited to, "hard disks, floppy disks, optical disks, flash memory devices, and magnetic tape, whether fixed, portable, or removable." A search of such sources and production of such data is overly broad, unduly burdensome, and not calculated to lead to the discovery of admissible evidence.

6. Lilly objects to Instruction Number 13 to the extent that it imposes burdens on Lilly beyond its obligations under the Federal Rules of Civil Procedure.

SPECIFIC OBJECTIONS TO REQUESTS FOR PRODUCTION

2ND SET, RFP NO. 1:

Please produce the results, summaries, and/or presentations concerning market surveys and/or focus groups for PROZAC that mention, measure, or refer to WITHDRAWAL or discontinuation symptoms.

OBJECTIONS TO 2ND SET, RFP NO. 1:

Lilly objects to this Request as overly broad and unduly burdensome as to time and scope and to the extent it seeks documents previously produced by Lilly in productions to which Plaintiff has access. Lilly also objects to this Request as it is not limited to documents relating to Cymbalta and therefore seeks information that is neither relevant nor likely to lead to the discovery of admissible evidence. The Complaint does not allege that Plaintiff was treated with Prozac. As such, documents relating to Prozac/fluoxetine are irrelevant in this matter. Subject to the foregoing objections, Lilly will produce results, summaries, or presentations of market surveys and/or focus groups for Prozac that mention, measure, or refer to discontinuation-emergent adverse events and that can be located through a reasonably diligent search of Lilly's Singlepoint market research database.

2ND SET, RFP NO. 2:

Please produce all marketing plans, market analyses, pricing studies, patient segmentation studies, conjoint studies / discrete choice studies, and/or any form of marketing evaluation of PROZAC that mention or discuss the issue of WITHDRAWAL or discontinuation symptoms.

OBJECTIONS TO 2ND SET, RFP NO. 2:

Lilly objects to this Request as overly broad and unduly burdensome as to time and scope and to the extent it seeks documents previously produced by Lilly in productions to which Plaintiff has access. Lilly also objects to this Request as it is not limited to documents relating to

Cymbalta and therefore seeks information that is neither relevant nor likely to lead to the discovery of admissible evidence. The Complaint does not allege that Plaintiff was treated with Prozac. As such, documents relating to Prozac/fluoxetine are irrelevant in this matter. Subject to the foregoing objections, Lilly will produce market analyses, pricing studies, conjoint studies / discrete choice studies, or other market evaluations for Prozac that mention or discuss discontinuation-emergent adverse events and that can be located through a reasonably diligent search of Lilly's Singlepoint market research database.

2ND SET, RFP NO. 3:

Please produce all marketing and/or sales documents that discuss, mention, or compare the WITHDRAWAL profile of Prozac to other antidepressants, including but not limited to CYMBALTA, Zoloft, Effexor, Paxil, Celexa, and Lexapro.

OBJECTIONS TO 2ND SET, RFP NO. 3:

Lilly objects to this Request as overly broad and unduly burdensome as to time and scope and to the extent it seeks documents previously produced by Lilly in productions to which Plaintiff has access. Lilly also objects to this Request as it is not limited to documents relating to Cymbalta and therefore seeks information that is neither relevant nor likely to lead to the discovery of admissible evidence. The Complaint does not allege that Plaintiff was treated with Prozac. As such, documents relating to Prozac/fluoxetine as compared to other, non-Cymbalta antidepressants are irrelevant in this matter. Subject to the foregoing objections, Lilly directs Plaintiff to its responses to 2nd Set, RFP No. 1 and 2nd Set, RFP No. 2.

2ND SET, RFP NO. 4:

Please produce all DOCUMENTS reflecting the amount of compensation, including but not limited to direct payments and stock options, given to the following current and/or former Lilly employees: Michael Detke, David Perahia, Sharon Hoog, Steven Knowles, Sara Mescher, Nayan Acharya, Mark Bangs, Greg Brophy, Bryan Boggs, Anne Sakai-Robbins, John Hixon, Antonio Crucitti, Madeleine Wohlreich, Matt Kuntz, Isabelle Murray, Torkil Fredborg, and Carol Stephens.

OBJECTIONS TO 2ND SET, RFP NO. 4:

Lilly objects to this Request as unduly infringing on the privacy rights of its employees and former employees. The precise dollar amounts of Lilly's compensation to its employees are not relevant to this litigation and Plaintiff's request would cause undue annoyance and embarrassment to these employees. *See* Minutes of Plaintiffs' Ex Parte Application to Compel Disclosure of the Financial Biases of Lilly Corporate Witnesses Who Will Testify at Trial, *Hexum v. Eli Lilly & Co.*, No. 2:13-cv-02701-SVW-MAN, dkt. 272 (C.D. Cal. Apr. 28, 2015).

Respectfully Submitted,

Dated: April 29, 2015

By: */s/ Jeffrey T. Bozman*

Jeffrey T. Bozman (83679)
Covington & Burling LLP
One CityCenter
850 Tenth Street, NW
Washington, DC 20001
Tel: (202) 662-5829
Fax: (202) 778-5829
jbozman@cov.com
Counsel for Eli Lilly and Company

CERTIFICATE OF SERVICE

I, Jeffrey T. Bozman, hereby certify that on the 29th day of April, 2015, I have served Plaintiff's counsel in this action with a copy of Defendant's Objections to Plaintiff's Second Set of Requests for Production by mailing a copy of the same by United States Mail, postage prepaid, and electronic mail to the following address:

Peter A. Miller
Miller Legal LLC
175 S. Pantops Drive, Third Floor
Charlottesville, VA 2291
Telephone (434) 529-6909
Facsimile (888) 830-1488
PMiller@MillerLegalLLC.com
Counsel for Janine Ali

Dated: April 29, 2015

By: */s/ Jeffrey T. Bozman*
Jeffrey T. Bozman (83679)
Covington & Burling LLP
One CityCenter
850 Tenth Street, NW
Washington, DC 20001
Tel: (202) 662-5829
Fax: (202) 778-5829
jbozman@cov.com
Counsel for Eli Lilly and Company

EXHIBIT 16

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF VIRGINIA
ALEXANDRIA DIVISION

JANINE ALI Plaintiff, v. ELI LILLY AND COMPANY, an Indiana corporation, Defendant.	CASE NO.: 1:14-CV-01615

DEFENDANT'S RESPONSES TO PLAINTIFF'S SECOND SET OF REQUESTS FOR PRODUCTION OF DOCUMENTS

Defendant Eli Lilly and Company ("Defendant" or "Lilly") hereby submits its responses to Plaintiff's Second Set of Requests for Production, as follows:

GENERAL STATEMENT

The following responses are subject to Lilly's Objections to Plaintiff's Second Set of Requests for Production served on April 30, 2015 pursuant to Federal Rule of Civil Procedure 34 and Local Civil Rule 26 and, for the sake of brevity, not repeated herein. Lilly has not fully completed its investigation of the facts relating to this case, its discovery, or its preparation for trial. Both discovery and independent investigation are ongoing. Therefore, all responses contained herein are based solely upon such information and documents as are both presently available and specifically known to Lilly. Lilly reserves the right to supplement these responses as discovery and this investigation proceed. Lilly's responses are in accordance with the requirements of the Federal Rules of Civil Procedure, the Local Rules, and any applicable Court Orders.

SPECIFIC RESPONSES TO REQUESTS FOR PRODUCTION

2ND SET, RFP NO. 1:

Please produce the results, summaries, and/or presentations concerning market surveys and/or focus groups for PROZAC that mention, measure, or refer to WITHDRAWAL or discontinuation symptoms.

RESPONSES TO 2ND SET, RFP NO. 1:

Subject to and without waiving its Objections to Plaintiff's Second Set of Requests for Production, Lilly will produce results, summaries, or presentations of market surveys and/or focus groups for Prozac that mention, measure, or refer to discontinuation-emergent adverse events and that can be located through a reasonably diligent search of Lilly's Singlepoint market research database.

2ND SET, RFP NO. 2:

Please produce all marketing plans, market analyses, pricing studies, patient segmentation studies, conjoint studies / discrete choice studies, and/or any form of marketing evaluation of PROZAC that mention or discuss the issue of WITHDRAWAL or discontinuation symptoms.

RESPONSES TO 2ND SET, RFP NO. 2:

Subject to and without waiving its Objections to Plaintiff's Second Set of Requests for Production, Lilly will produce market analyses, pricing studies, conjoint studies / discrete choice studies, or other market evaluations for Prozac that mention or discuss discontinuation-emergent adverse events and that can be located through a reasonably diligent search of Lilly's Singlepoint market research database.

2ND SET, RFP NO. 3:

Please produce all marketing and/or sales documents that discuss, mention, or compare the WITHDRAWAL profile of Prozac to other antidepressants, including but not limited to CYMBALTA, Zoloft, Effexor, Paxil, Celexa, and Lexapro.

RESPONSES TO 2ND SET, RFP NO. 3:

Subject to and without waiving its Objections to Plaintiff's Second Set of Requests for Production, Lilly directs Plaintiff to its responses to 2nd Set, RFP No. 1 and 2nd Set, RFP No. 2.

2ND SET, RFP NO. 4:

Please produce all DOCUMENTS reflecting the amount of compensation, including but not limited to direct payments and stock options, given to the following current and/or former Lilly employees: Michael Detke, David Perahia, Sharon Hoog, Steven Knowles, Sara Mescher, Nayan Acharya, Mark Bangs, Greg Brophy, Bryan Boggs, Anne Sakai-Robbins, John Hixon, Antonio Crucitti, Madeleine Wohlreich, Matt Kuntz, Isabelle Murray, Torkil Fredborg, and Carol Stephens.

RESPONSES TO 2ND SET, RFP NO. 4:

Lilly refers Plaintiff to its objections to this Request.

Respectfully Submitted,

Dated: May 15, 2015

By: */s/ Jeffrey T. Bozman*
Jeffrey T. Bozman (83679)
Covington & Burling LLP
One CityCenter
850 Tenth Street, NW
Washington, DC 20001
Tel: (202) 662-5829
Fax: (202) 778-5829
jbozman@cov.com
Counsel for Eli Lilly and Company

CERTIFICATE OF SERVICE

I, Jeffrey T. Bozman, hereby certify that on the 15th day of May, 2015, I have served Plaintiff's counsel in this action with a copy of Defendant's Responses to Plaintiff's Second Set of Requests for Production by electronic mail to the following address:

Peter A. Miller
Miller Legal LLC
175 S. Pantops Drive, Third Floor
Charlottesville, VA 2291
Telephone (434) 529-6909
Facsimile (888) 830-1488
PMiller@MillerLegalLLC.com
Counsel for Janine Ali

Dated: May 15, 2015

By: */s/ Jeffrey T. Bozman*
Jeffrey T. Bozman (83679)
Covington & Burling LLP
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850 Tenth Street, NW
Washington, DC 20001
Tel: (202) 662-5829
Fax: (202) 778-5829
jbozman@cov.com
Counsel for Eli Lilly and Company

EXHIBIT 17

Wisner, R. Brent

From: Wisner, R. Brent
Sent: Tuesday, May 19, 2015 12:43 PM
To: Stekloff, Brian; Imbroscio, Michael
Cc: Pete Miller
Subject: Prozac Production and Rule 30(b)(6) Deposition
Attachments: CYM-02990295.pdf

Brian,

I have reviewed the document production relating to Prozac. I have a few questions:

1. There are no documents prior to 1999. Prozac was on the market for years, starting in the late 1980s. Why are there no documents prior to 1999?
2. There is not a single marketing plan for Prozac, i.e., documents akin to the Brand Counsel documents produced for Cymbalta. Why?
3. There are no examples of sales aids used by Prozac sales representatives. Why?
4. I've attached a document, CYM-02990295, which appears to be the results of a search of Lilly's SinglePoint database. Were all the documents listed in the results produced? Again, is there a reason that no documents are dated earlier than 2001?

Are you free to talk about this production and the recent 30(b)(6) notice today?

Thanks,

R. Brent Wisner, Esq.
BAUM, HEDLUND, ARISTEI & GOLDMAN, P.C.
12100 Wilshire Blvd, Suite 950
Los Angeles, CA 90025
Direct: 310-820-6294
Office: 310-207-3233
Fax: 310-820-7444
RBWisner@BaumHedlundLaw.com
www.BaumHedlundLaw.com

EXHIBIT 18

Wisner, R. Brent

From: Wisner, R. Brent
Sent: Thursday, May 21, 2015 12:14 PM
To: 'Stekloff, Brian'; Pete Miller; T. Matthew Leckman
Cc: Imbroscio, Michael; Jones, Phyllis; Reynolds, Brett
Subject: RE: Ali and Hagan-Brown: Second 30(b)(6) Notice

Brian,

Since discovery is closing on May 29, 2015, I was hoping Lilly would cooperate and allow the 30(b)(6) deposition to happen. But, as in almost every other aspect of discovery in these cases, Lilly refuses to comply with a simple discovery request and will force Plaintiffs to file a motion. While I disagree with Lilly's position—Lilly's marketing of Prozac relating to withdrawal is clearly relevant to Lilly's knowledge and motive in misrepresenting Cymbalta's withdrawal risks—there is simply not enough time to file a motion to compel and take the deposition before the close of discovery in *these* cases. For the *Ali* and *Hagan-Brown* cases, I formally withdrawal the 30(b)(6) with regard to Prozac marketing, although I fully intend to pursue it in another one of the dozens of cases we have pending in other courts, where discovery is not quickly approaching a cutoff.

Notwithstanding, Lilly's refusal to produce documents is unacceptable. I will be filing a motion to compel production of documents relating to Requests for Production Nos. 1, 2, and 3 of Plaintiffs' Second Set of Requests for Production. I will file the motion by tomorrow and will notice it for a hearing on May 29, 2015.

I plan to file the following documents which have been designated confidential along with the motion (note there will be other documents filed, but they are not designated confidential):

CYM-01813088
CYM-R-01873414 (note, the redacted version is already de-designated)
CYM-02989901
CYM-02786215
CYM-02784115
CYM-02806828
FAVA-001-*011
FAVA-025-*043
Perahia Depo at 111-114
Detke Depo at 19-20, 100-101, 181-183
Hoog Depo at 69-74, 85-91

Thanks,

Brent

From: Stekloff, Brian [mailto:BStekloff@cov.com]
Sent: Wednesday, May 20, 2015 8:28 PM

To: Wisner, R. Brent; Pete Miller; T. Matthew Leckman
Cc: Imbroscio, Michael; Jones, Phyllis; Reynolds, Brett
Subject: FW: Ali and Hagan-Brown: Second 30(b)(6) Notice

Brent:

Following up on our discussion yesterday, for the reasons described below, we do not agree that additional Prozac-related discovery is appropriate, relevant, or timely. We cannot agree to produce additional documents, a 30(b)(6) witness, or respond to additional RFAs. We intend on filing a motion to quash the second 30(b)(6) notice unless you withdraw the notice.

To be clear, consistent with our discussion yesterday, we will consider stipulating to the authenticity of the documents you sent us by bates number earlier today. We are in the process of pulling those documents and will update you on our position as soon as we have reviewed them.

Brian

Brian Stekloff

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COVINGTON

From: Stekloff, Brian
Sent: Monday, May 18, 2015 9:40 PM
To: 'Wisner, R. Brent'; 'Pete Miller'; 'T. Matthew Leckman'
Cc: Imbroscio, Michael; Jones, Phyllis; Reynolds, Brett
Subject: Ali and Hagan-Brown: Second 30(b)(6) Notice

Brent:

We have received your second 30(b)(6) deposition notice in the *Ali* and *Hagan-Brown* cases and intend on filing a motion to quash. Before we do so, and given the looming close of discovery, we wanted to make you aware of our position on this issue.

First, Prozac Marketing is not relevant to this litigation. Simply put, this litigation is about Cymbalta and your recent efforts to obtain discovery regarding Prozac are inappropriate and burdensome. Moreover, in these two cases, Prozac is particularly irrelevant given that neither of your clients ever used Prozac, relied on Prozac marketing, or even relied on Cymbalta marketing.

Second, it is unnecessary and burdensome to seek the deposition of a Custodian of Records. Your notice indicates that you would like to ask a deponent about the authenticity of documents produced by Lilly in discovery. We are happy to consider a stipulation on this issue, reserving our right to challenge admissibility of any such documents in any trial. Moreover, in the *Mayes* case, you recently served an interrogatory on this exact issue--Interrogatory No. 1--that we intend on responding to in due course and pursuant to the deadlines in that case.

Third, although we jointly moved to extend the discovery deadline in these cases, we believe the clear intent of that motion, as demonstrated by the grounds described in the motion, was to allow the parties to fulfill our existing discovery obligations; not to notice wholly new requests at the close of the original discovery deadline. For this reason, we believe your second 30(b)(6) notice is inappropriate and untimely.

Finally, you do not have the right to serve a second 30(b)(6) notice. Pursuant to Rule 30(a)(2)(B), a party must obtain leave of court to reexamine a person who has already been deposed in a case. Fed. R. Civ. P. 30(a)(2)(B). This requirement also applies to depositions conducted under Rule 30(b)(6); a second deposition of a corporate entity requires leave of court. *Ameristar Jet Charter, Inc. v. Signal Composites, Inc.*, 244 F.3d 189, 192 (1st Cir. 2001); *see also State Farm Mut. Auto. Ins. Co. v. New Horizont, Inc.*, 254 F.R.D. 227 (E.D. Pa. 2008); *Walker v. State Farm Mut. Auto. Ins. Co.*, 2012 WL 1155140, at *9 (S.D.W.Va. Apr. 5, 2012); *In re Sulfuric Acid Antitrust Litig.*, 2005 WL 1994105 (N.D. Ill. Aug. 19, 2005). Even if Plaintiffs were to request leave from the Court, moreover, this second deposition is not permissible. Plaintiffs have "had ample opportunity to obtain the information by discovery in the action." Fed. R. Civ. P. 26(b)(2). Drafting seratim notices to force Lilly to appear for multiple 30(b)(6) depositions constitutes a "'wait-and-see' approach to discovery" that is not contemplated by the Federal Rules and improperly shifts costs to Lilly. *See State Farm*, 254 F.R.D. at 235-36.

For these reasons, we ask that you withdraw your second 30(b)(6) notice immediately. We reserve the right to seek costs associated with the filing of any motion to quash. We are available to discuss at your convenience.

Brian

Brian Stekloff

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COVINGTON

EXHIBIT 19

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

ERIN HEXUM and NICK HEXUM,

Plaintiffs,

-vs-) CIVIL ACTION NO.
) CV 13-2701-SVW-MAN

ELI LILLY & COMPANY, an Indiana Corporation,

Defendant.

CLAUDIA HERRERA and PETER LOWRY,

Plaintiffs,

-vs-) CIVIL ACTION NO.
) CV 13-2702-SVW-MAN

ELI LILLY & COMPANY, an Indiana Corporation,

Defendant.

VIDEOTAPED DEPOSITION OF SHARON L. HOOG, M.D.

CONFIDENTIAL

The videotaped deposition upon oral examination of SHARON L. HOOG, M.D., a witness produced and sworn before me, Janine A. Ferren, RPR, CRR, CSR No. 93-R-1028, Notary Public in and for the County of Hamilton, State of Indiana, taken on behalf of the Plaintiffs, at the offices of Connor Reporting, 1650 One American Square, Indianapolis, Marion County, Indiana, on the 10th day of December, 2014, at 10:00 a.m., pursuant to the Federal Rules of Civil Procedure with written notice as to time and place thereof.

Q And then you have spent the last 22 years as an employee of the defendant Eli Lilly & Company; is that right?
A That's right.
Q You started at Lilly back in 1992, if I have my timeline correct?
A Uh-hum, that's right.
Q You started out as a clinical research physician; right?
A Yes.
Q And in 1994 you became a research scientist?
A Yes.
Q In 1998 you became a medical advisor?
A Correct.
Q Tell our jury, what is a medical advisor?
A In the drug development teams, there are representatives of several disciplines, for example, statistics, toxicology, clinical pharmacology, and medical. And as a physician, I was giving medical input to decisions that had to take in a number of different scientific aspects.
Q Are you finished?
A Pardon me?
Q I'm sorry. Are you finished? I didn't want to

cut you off.
A Uh-hum, I'm finished.
Q So if I understand correctly, you -- when you became a medical advisor in 1998, you held that position roughly until 2006; is that right?
A That's correct.
Q And certainly during that time, as we know from these lawsuits, you were a medical advisor spanning some of the time that Cymbalta or duloxetine was in development and eventually launched in the United States; correct?
A Could you please repeat that?
Q Sure. Let me do it piece by piece.
Duloxetine or Cymbalta was developed and eventually brought to launch in the United States in 2004; correct?
A Correct.
Q And so that was during your time as a medical advisor; right?
A That -- right. I was working in regulatory affairs as a medical advisor.
Q Okay. Did you have response- -- that's what I'm driving at. Did you have responsibilities with respect to Cymbalta specifically during your

that fair to say?
A I don't know how to quantify my contribution to success.
Q Well, I don't want you to quantify it. What I'm asking is simply whether, I guess, qualitatively, you would agree that you played some role in the development and brand success of Cymbalta over the course of its decade, near-decade on the market?
A Never has brand success been a part of my intention or job description.
Q You've conducted some research and published some peer-reviewed literature relating to both Cymbalta and Prozac; right?
A Yes.
Q In fact, you've published in a peer-reviewed literature on Prozac dating back to the late '90s, I think; is that right?
A I don't recall when that was published, but yeah.
Q We're going to look at some documents that may refresh your memory. But generally speaking you recall doing some research relating to Prozac and some other earlier antidepressants back in the early '90s; true?

A True.
Q And your research and peer-review publications continued on into post-2000 and post-2004 when Cymbalta was launched; true?
A With respect to Prozac, you're saying?
Q Well, with respect to Prozac and eventually Cymbalta; is that right?
A Could you please ad- -- repeat what the question was about those two?
Q Sure. Did you publish on Prozac?
A Yes.
Q Have you published on Cymbalta?
A Yes.
Q Have you been publishing in the peer-reviewed literature, over the course of the years and up to our time here today, back to 1990s? Is that a fair span of your time publishing in the literature?
A No. I have not published since I left in 2005.
Q Did you publish a paper on Cymbalta relating to pregnancy?
A Oh, right. Sorry about that.
Q When was that?
A I don't recall.

Q Yeah, and I don't -- I didn't intend to ask you about it, so I don't even know that I have it in your binder. But you do recall publishing a paper on Cymbalta and pregnancy much more recently than 2005; right?
A Correct.
Q And as far as I can tell, you were still publishing on Prozac as late as 2006; is that -- does that ring a bell? Is that fair to say?
A I don't recall.
Q Okay. So if I told you that -- and I can send a copy of this. I don't -- I have but one in front of me because I didn't expect to ask you about it. But if I told you that there was a paper entitled, "Duloxetine and Pregnancy Outcomes: Safety Surveillance Findings" authored by you and Drs. Cheng, Elpers, and Dowsett in the International Journal of Medical Sciences, does that ring a bell?
A Yes.
Q If I told you that was published in 2013, would you -- does that ring -- does that refresh your memory?
A I don't remember it being that late.
Q I've got Volume 10, 2013, of this journal. I

don't want to take away from what -- where I'm heading here with my questioning, but at the break I'll be happy to send you a copy and you can confirm that I'm not lying to you about publication dates.

If you turn -- and I'm not going to mark this for the record, but if you tab -- turn to Tab 3E, 3E as in echo, this is a paper that appeared in 2006 in the Journal of Child and Adolescent Psychopharmacology; correct?

A Correct.

Q It's entitled, "Fluoxetine 40 to 60 milligrams versus fluoxetine 20 milligrams in the treatment of children and adolescents with a less-than complete response to nine-week treatment with fluoxetine 10 to 20 milligrams: A pilot study."

Did I read that correctly as the title?

A Yes.

Q The first two authors listed here in this 2006 paper -- by the way, fluoxetine is Prozac, for our jury's benefit; correct?

A Correct.

Q Prozac was the antidepressant available, modern antidepressants available in the United States market; correct?

A Yes.
Q And you know that because you did, again, some research as early as the mid-to-late 1990s on Prozac and other antidepressants; right?
A Could you please repeat that question?
Q You're aware that Prozac was one of the earliest, if not the earliest anti- -- modern antidepressant available in the United States, because you were doing research on Prozac back in the mid to late 1990s; right?
A Correct. It was the first serotonin reuptake inhibitor approved in the United States.
Q Right. I didn't want to say it first because I wasn't sure off the top, but my memory is that it was the very first in the United States; right?
A In this country, yeah.
Q And that's also an Eli Lilly product; right?
A Yes.
Q And so what I'm trying to do is the timeline for your jury, this 2006 Prozac paper, you were the second author listed on this paper; right?
A Right.
Q And so is it fair to say that, over the course of the years, your Prozac and Cymbalta

publications and research have continued?
A Yes.
Q And I don't want to put words in your mouth, I know you don't want to quantify how much of a role you've had in the success of either product. But is it fair to say it's been a central focus of your time at Lilly to work on both Prozac and later Cymbalta in various roles and responsibilities?
A Particular, yes, in the earlier years.
Q As we've seen, Cymbalta has been a huge source of revenue for Eli Lilly & Company; correct?
A Correct.
Q As a matter of fact, is it true that when Lilly believes that Cymbalta will not be profitable for the company, it doesn't even bother to pursue it in a given country?
A I --
MS. JONES: I'm sorry. Objection to the form.
Q I'm asking you if it's true. Do you know whether or not that's true?
MS. JONES: Same objection.
A I'm not involved in the decision about where to launch or why.

Q Can we agree that it should always put safety over profits?
A Yes.
MR. LECKMAN: What I had intended to be marked before we got back on the record was Exhibit 7, which is, I think, the number that we're up to. And my apologies again to the court reporter that she does not have a copy in front of her. But Dr. Hoog and counsel, you have a copy in front of you in your binder, and that tab in your binder is Tab 8.
(Deposition Exhibit 7 marked for identification.)
MS. JONES: I think we're set, Matt.
MR. LECKMAN: Okay.
Q I just wanted to be sure that you were -- you were ready, Doctor.
So I'll represent for the record that what we've marked as Exhibit 7 are some documents and materials that were produced in the course of discovery by a gentleman by the name of Maurizio Fava, or Dr. Maurizio Fava.
You know Dr. Fava; correct?
A I do.
Q We -- I'll further represent for the record that

plaintiffs, in the course of discovery of these lawsuits, has subpoenaed some of these documents from Dr. Fava. And as I understand, how they got into this sequence, the -- a copy of these was also produced to defendant Eli Lilly & Company who put these Bates numbering and confidential and protective order notation on the bottom. So these are ordered in the sequence that I believe they were produced to us. I'll refer during our discussion to the bottom right-hand Bates number, FAVA 001 all the way through FAVA 143 -- I'm sorry, FAVA 144.

A Okay.

Q And again, Doctor, these are a collection of materials that were produced pursuant to a subpoena to Dr. Fava where we requested that he give us certain materials relating to his involvement with Lilly and studies that he conducted along with your company. And certainly that's familiar to you because you participated in authorship of some of those papers; right?

A Right.

Q And again, this is what we were alluding to earlier when we were talking about your

involvement with Prozac dating back to the 1990s; is that right?

A Yes, that would be -- that's -- that's how you described it.

Q So I want to ask you some questions about -- we're not going to look through this entire set, but there are a few items that I want to take a look at. Certainly if you feel like you need a broader context, you're free to tell me, you know, "Stop the presses," go off the record, and you can review the whole thing. But I'm going to focus my questioning to a couple of discrete sections of this collection; okay?

A Okay.

Q At FAVA 002, there is a -- what appears to me to be a memo from a gentleman by the name of William Krebs; correct?

A Correct.

Q And William Krebs was also an Eli Lilly employee; correct?

A Correct.

Q What was William Krebs' position in the company at the time?

A He was a contracted statistician, I believe he

was contracted.
Q Medical doctor?
A No.
Q In any event, this is a memo from William Krebs to Sharon Blomgrem. That's you, that's your maiden name; correct?
A Actually, that was my married name. Hoog is my --
Q Oh, I'm sorry.
A -- given name.
Q Hoog is a better name.
So Sharon Blomgrem was you in 1997?
A Correct.
Q Okay. And it's also addressed to Cris Nordhoff; correct?
A Correct.
Q Who is Cris Nordhoff?
A I don't recall what her title would have been, but she was involved in -- yeah.
Q She was a Lilly employee?
A Yes.
Q And by the way, at the time you were a Lilly employee as well; correct? This is back when you were a medical advisor?
A I was a CRP, I think, a clinical research

physician.

Q Oh, I see, yeah, okay.

So you were -- well, it looks like on your resume, you say you were a research scientist from June '94 to August '98, and that would span this time. So you think you were a clinical research physician or a research scientist at this time?

A This is confusing to me, too, but the titling of different positions and which, you know, pay scale they fit into is changing. My role was as a physician.

Q Okay, yeah. If I just want to give you an opportunity to finish. I'm not trying to confuse you with your resume.

Did you prepare your resume or did somebody else prepare it for you?

A Oh, I prepared it, and I cross-checked it with HR.

Q Fair enough.

A Because in my world -- I'll stop.

Q And copied on this memo from William Krebs to you and Cris Nordhoff was a gentleman by the name of Michael Wilson and then also someone named Lee Harrington.

Who were Wilson and Harrington?

A Wilson was another statistician, and I don't recall what Lee Harrington did.

Q Fair enough. All Lilly employees are on this memo, in other words?

A Yes.

Q And this memo is dated June 27, 1997; correct?

A Yes.

Q And I'm not going to go through every line of the memo, but certainly take a minute to familiarize or refamiliarize yourself with it. This is the memo that you received in June of 1997, whatever your position may have been at the company, in your capacity as a physician relating to some research that was being done on Prozac; correct?

A Correct.

Q Is it fair to say that a part of the research that Lilly was doing relating to Prozac and a part of the research that you had a hand in was comparing Prozac to other SSRIs in the class or other antidepressants in the class?

A Yes.

Q And the comparison was to attempt to differentiate fluo- -- I'm sorry, fluoxetine

or Prozac in terms of efficacy and safety as well; is that fair -- a fair summation?

A Yes.

Q And the better the research could show Prozac efficacy, the better off for the drug, obviously, correct, and the company?

A Well, that's always in a balance with what you have to or what might be your risks, you know, on the adverse events side. I mean, that balance has to be right.

Q Sure. I was going to get to that side of the balance in a second. But they're both, I guess, kind of symbiotic, in other words?

A Well, there's always a relative efficacy and a relative safety or tolerability kind of feature to the experience of taking a medicine. I don't know that they're symbiotic.

Q And in the end analysis of any particular set of research that's being done for any drug, the better off that drug performs in terms of efficacy, the better for the drug in the market; is that fair?

A Only if it has a proportionally acceptable safety profile.

EXHIBIT 20

UNITED STATES DISTRICT COURT

CENTRAL DISTRICT OF CALIFORNIA

WESTERN DIVISION

SIDNEY CARTER, PLAINTIFF, V. ELI LILLY AND COMPANY, ET AL., DEFENDANTS.	CV 13-2700-GHK(FFMX)
ERIN HEXUM, ET AL., PLAINTIFFS, V. ELI LILLY AND COMPANY, ET AL., DEFENDANTS.	CV 13-2701-GHK(FFMX)
CLAUDIA HERRERA, ET AL., PLAINTIFFS, V. ELI LILLY AND COMPANY, ET AL., DEFENDANTS.	CV 13-2702-GHK(FFMX) LOS ANGELES, CALIFORNIA SEPTEMBER 9, 2014 (10:04 A.M. TO 10:15 A.M.) (10:57 A.M. TO 11:05 A.M.)

HEARING

BEFORE THE HONORABLE FREDERICK F. MUMM
UNITED STATES MAGISTRATE JUDGE

PROCEEDINGS RECORDED BY ELECTRONIC SOUND RECORDING;
TRANSCRIPT PRODUCED BY TRANSCRIPTION SERVICE.

APPEARANCES:	SEE NEXT PAGE
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I N D E X

CV 13-2700-GHK(FFMX) SEPTEMBER 9, 2014
CV 13-2701-GHK(FFMX)
CV 13-2702-GHK(FFMX)

PROCEEDINGS: DEFENDANT'S MOTION FOR PROTECTIVE ORDER

LOS ANGELES, CALIFORNIA; TUESDAY, SEPTEMBER 9, 2014; 10:04 A.M.

THE CLERK: ALL RISE AND COME TO ORDER.

THE HONORABLE FREDERICK F. MUMM, UNITED STATES MAGISTRATE JUDGE, PRESIDING.

PLEASE BE SEATED.

CALLING ITEM NUMBER 3, CV 13-2700, SIDNEY CARTER VERSUS ELI LILLY AND COMPANY; CASE NUMBER CV 13-2701, ERIN HEXUM VERSUS ELI LILLY AND COMPANY; CASE CV 13-2702, CLAUDIA HERRERA VERSUS ELI LILLY AND COMPANY.

APPEARANCES, PLEASE.

MR. LECKMAN: GOOD MORNING, YOUR HONOR.

MATT LECKMAN HERE ON BEHALF OF THE PLAINTIFFS.

THE COURT: GOOD MORNING.

MS. JONES: GOOD MORNING, YOUR HONOR.

PHYLLIS JONES ON BEHALF OF ELI LILLY AND COMPANY.

THE COURT: GOOD MORNING.

PLEASE BE SEATED.

THIS IS A MOTION FOR PROTECTIVE ORDER FILED BY ELI LILLY.

I BELIEVE WE'VE ALREADY RESOLVED THE ISSUES RELATING TO THE DEPOSITIONS; IS THAT CORRECT?

MS. JONES: THAT'S CORRECT, YOUR HONOR.

WE APPRECIATE YOU GIVING THE PARTIES THE OPPORTUNITY TO HEAR FROM YOU ON THE TELEPHONIC CONFERENCE, BUT WE HAVE MOVED FORWARD WITH THE DEPOSITIONS --

THE COURT: ALL RIGHT.

MS. JONES: -- CONSISTENT WITH YOUR GUIDANCE.

THE COURT: OKAY.

ALL RIGHT. SO, THERE ARE ISSUES REGARDING REQUEST FOR PRODUCTION, A 30(B)(6) DEPOSITION CATEGORIES AND A THIRD-PARTY SUBPOENA.

ALL OF THE ISSUES RELATE TO THE DISCOVERABILITY OF INFORMATION RELATED TO WITHDRAWAL SYMPTOMS OF DRUGS OTHER THAN CYMBALTA, THE DRUG WHICH IS AT ISSUE IN THIS CASE.

LILLY CONTENDS THAT SYMPTOMS RELATED TO DISCONTINUATION OF PROZAC ARE IRRELEVANT BECAUSE PLAINTIFFS DID NOT TAKE PROZAC AND PROZAC IS A DIFFERENT CLASS OF DRUG FROM CYMBALTA -- THAT IS, PROZAC IS AN SSRI AS OPPOSED TO AN SNRI.

LILLY ALSO CONTENDS THAT IT WOULD BE BURDENSOME TO RESPOND TO DISCOVERY REGARDING PROZAC.

AS I UNDERSTAND IT, PLAINTIFFS' THEORY APPEARS TO BE THAT LILLY PREVIOUSLY SPONSORED STUDIES ON SYMPTOMS ASSOCIATED WITH STOPPING THE USE OF SSRI'S AND SNRI'S. THESE STUDIES COMPARED AT LEAST PROZAC, PAXIL AND ZOLOFT, WHICH ARE SSRI'S, AND EFFEXOR, WHICH IS AN SNRI.

THESE STUDIES SHOWED A CORRELATION BETWEEN THE FREQUENCY OF WITHDRAWAL SYMPTOMS AND THE HALF-LIFE OF THE DRUG. MOREOVER, LILLY TOUTED ITS DRUG PROZAC AS HAVING A RELATIVELY LONG HALF-LIFE AND SUGGESTED THAT THE LONG HALF-LIFE WOULD BE EXPECTED TO RESULT IN LESS FREQUENT APPEARANCE OF WITHDRAWAL

SYMPTOMS.

NOW LILLY IS MARKETING CYMBALTA WHICH HAS A RELATIVELY SHORT -- A RELATIVELY SHORT HALF-LIFE. LILLY SPONSORED A STUDY REGARDING WITHDRAWAL SYMPTOMS OF CYMBALTA THAT USED A DIFFERENT METHOD OF OBTAINING INDICATIONS OF WITHDRAWAL SYMPTOMS THAN USED IN THE EARLIER STUDIES. SPECIFICALLY, RATHER THAN SYSTEMATIC MONITORING WITH A CHECKLIST TO RECORD SYMPTOMS, IT RELIED ON SPONTANEOUS REPORTS FROM STUDY SUBJECTS. PLAINTIFF CONTENDS THIS METHOD RESULTED IN LOWERING REPORTING OF WITHDRAWAL SYMPTOMS.

FROM THE FOREGOING, I FIND THAT IT IS AT LEAST ARGUABLE THAT THESE CLASSES OF REUPTAKE INHIBITORS, WHETHER SSRI'S OR SNRI'S, POSE SIMILAR RISKS UPON DISCONTINUATION. THE MECHANISMS OF THE SSRI'S AND SNRI'S ARGUABLY ARE SIMILAR. ALTHOUGH, SNRI'S OBVIOUSLY INHIBIT THE REUPTAKE OF NOREPINEPHRINE AS WELL AS SEROTONIN WHEREAS THE SSRI'S PRIMARILY INHIBIT THE REUPTAKE OF SEROTONIN.

I ALSO FIND THAT IT IS AT LEAST ARGUABLE THAT LILLY'S KNOWLEDGE OF WITHDRAWAL RISKS AS DEMONSTRATED BY THE EARLIER STUDIES PLAYED A PART IN ITS EVALUATION OF CYMBALTA'S WITHDRAWAL RISKS AND COULD BE RELEVANT TO THE PUNITIVE DAMAGE ISSUE.

SO, BASED ON THOSE FINDINGS, MY TENTATIVE WOULD BE THAT THE PLAINTIFF IS ENTITLED TO THE INFORMATION THEY'RE SEEKING. I DO NOTE THAT SOME OF THE REQUESTS FOR PRODUCTION

PARTICULARLY ARE -- SEEM TO BE RATHER BROAD. AND I WOULD THINK IT WOULD BE APPROPRIATE FOR THE PARTIES TO MEET AND CONFER THIS MORNING TO WORK OUT WHETHER OR NOT THE DOCUMENT REQUEST COULD BE NARROWED TO FOCUS ON THE INFORMATION REGARDING SYMPTOMS OR FREQUENCY, INTENSITY, ET CETERA RELATED TO DISCONTINUATION OF SSRI'S AND SNRI'S.

WITH RESPECT TO ISSUE NUMBER TWO, IT DOES NOT APPEAR TO ME AT FIRST BLUSH THAT THE CATEGORIES ARE APPROPRIATE CATEGORIES FOR A DEPOSITION. IT SEEMS AS IF WHAT THE PLAINTIFF IS ASKING IS FOR THE DEFENDANT TO MEMORIZE THE LIST OF NAMES. I WOULD THINK THAT IT WOULD BE MORE APPROPRIATE JUST TO SEND INTERROGATORIES AS TO THAT ISSUE. AND, SO, I'D LIKE TO HEAR FROM THE PARTIES ON THAT.

AND AS TO ISSUE NUMBER THREE, THESE WOULD BE SUBPOENAS SERVED ON THIRD PARTIES. AND THE THIRD PARTIES HAVE NOT MOVED FOR A PROTECTIVE ORDER. I DON'T SEE THAT LILLY HAS CLAIMED THAT ANY OF THE REQUESTED INFORMATION IS PRIVILEGED. AND, SO, I WOULD THINK IT WOULD BE APPROPRIATE TO DENY THE PROTECTIVE ORDER WITH RESPECT TO ISSUE THREE.

SO, I WILL HEAR FROM THE PARTIES.

WHO WOULD LIKE TO GO FIRST?

(PAUSE IN PROCEEDINGS.)

MR. LECKMAN: I'M HAPPY -- I'M HAPPY TO GO --

(LAUGHTER.)

MR. LECKMAN: I HATE TO ACTUALLY SNATCH DEFEAT FROM

THE JAWS OF VICTORY, BUT, YOUR HONOR, I'LL SPEAK TO THE SECOND ISSUE FIRST RELATING TO THE -- THE 30(B)(6) REQUEST FOR THE RESEARCH SYMPOSIUM.

THE PLAINTIFFS ARE HAPPY TO TAKE A CLOSER LOOK AT THE CATEGORIES AND EITHER REFASHION IN A MORE APPROPRIATE MANNER FOR A 30(B)(6) OR MORE NARROWLY TAILORED SET OF CATEGORIES FOR A 30(B)(6) IF YOUR HONOR WOULD PERMIT THAT. ALTERNATIVELY, I CAN MEET AND CONFER WITH COUNSEL TO PUT THEM IN AN INTERROGATORY FORM.

AS TO THE REQUEST FOR PRODUCTION, I'D JUST ASK TO CLARIFY THAT WE'RE TALKING ABOUT 125, 140, AND 141.

I NOTED THAT YOUR HONOR MENTIONED THEY APPEAR TO BE BROAD. AND I WANT TO HAVE AN UNDERSTANDING AS TO WHAT YOUR HONOR WOULD DIRECT US AS TO WHAT YOU WOULD LIKE TO SEE NARROWED WITH -- WITH RESPECT TO THOSE REQUESTS.

THE COURT: ALL RIGHT. LET ME SEE WHERE THEY'RE LISTED HERE.

(PAUSE IN PROCEEDINGS.)

THE COURT: ALL RIGHT. JUST -- WELL, FOR INSTANCE, THE FIRST ONE, REQUEST NUMBER 125,

"ALL DOCUMENTS THAT REFER TO PROZAC OR
FLUOXETINE AND WITHDRAWAL,
DISCONTINUATION, DEPENDENCE OR ADDICTION."

I MEAN, THE FACT THAT IT JUST REFER -- IT SEEMS TO ME THERE MUST BE SOME WAY TO WORD THAT THAT IT'S REALLY GETTING

WHAT YOU'RE INTERESTED IN AND NOT JUST GETTING EVERYTHING THAT TALKS ABOUT PROZAC.

MR. LECKMAN: SO, IT'S NOT THE BEST-WORDED REQUEST I'VE EVER SENT. AND I'LL FIX THAT.

THE COURT: THAT'S SORT OF THE GIST OF WHAT I -- I THINK YOU CAN TELL FROM MY RULING THAT I -- I BELIEVE YOU'RE ENTITLED TO THE INFORMATION THAT YOU REALLY NEED TO INDICATE, YOU KNOW, WHAT -- WHAT LILLY KNEW ABOUT THESE WITHDRAWAL SYMPTOMS AND HOW THEY REACT WITH THESE -- WITH THE DISCONTINUATION OF REUPTAKE INHIBITORS.

MR. LECKMAN: WE'LL NARROW ACCORDINGLY. AND I'LL MEET AND CONFER ON -- ON THOSE ITEMS WITH DEFENSE AS WELL.

THE COURT: ALL RIGHT.

NOW, WITH RESPECT TO THE THIRD ISSUE, I GUESS YOU DON'T HAVE ANYTHING TO SAY ON THAT.

SO --

MR. LECKMAN: I'M GOING TO BE QUIET ON THAT ISSUE.

THE COURT: -- I'LL HEAR FROM MS. JONES.

(LAUGHTER.)

MS. JONES: THANK YOU, YOUR HONOR.

WE'LL OBVIOUSLY BE GUIDED BY YOUR HONOR'S DIRECTION WITH RESPECT TO ALL THE ITEMS THAT YOU'VE TOUCHED ON IN YOUR TENTATIVE RULING.

I WOULD JUST REITERATE WHAT WE'VE ARTICULATED IN OUR PAPERS, WHICH IS THIS IS ACTUALLY NOT A CASE WHERE THERE'S ANY

SERIOUS DISPUTE THAT LILLY WAS NOT AWARE OF THE POTENTIAL RISK OF DISCONTINUATION SYMPTOMS. IT'S A RISK THAT'S BEEN LABELED FOR THE PRODUCT SINCE ITS APPROVAL IN THE UNITED STATES FOR MAJOR DEPRESSIVE DISORDER IN 2004.

SO, WE MAY WELL GO THROUGH A FAIRLY COMPREHENSIVE ARCHEOLOGICAL DISCOVERY EXERCISE LOOKING FOR PROZAC DOCUMENTS AND MAY FIND OURSELVES WHERE WE ARE TODAY, NAMELY, THAT WE KNOW THAT THE COMPANY WAS AWARE OF THE RISK OF DISCONTINUATION SYMPTOMS, THAT IT LABELED ON THOSE SYMPTOMS.

AND WHETHER OR NOT THAT WILL MEANINGFULLY ADVANCE THE MERITS OF THE PLAINTIFFS' CLAIMS I THINK IS A VERY REAL QUESTION. SO, I THINK THERE IS A FAIRLY SERIOUS RELEVANCE ISSUE THAT'S BEFORE THE COURT CURRENTLY. AND, OF COURSE, THIS COULD POTENTIALLY INVOLVE A FAIRLY SIGNIFICANT DEVOTION OF RESOURCES AND DEVIATION OF RESOURCES BY THE PARTIES IN TERMS OF IDENTIFYING THE RELEVANT MATERIALS THAT WILL LIKELY BE IN BOTH HARD COPY AND ELECTRONIC FORM. AND, THEN, THAT WILL REQUIRE SOME FAIRLY DETAILED INVESTIGATION.

SO, WE'LL BE GUIDED BY YOUR HONOR'S -- YOUR HONOR'S DIRECTION, OBVIOUSLY. BUT I DO WANT TO JUST NOTE FOR THE RECORD THAT WE'RE TALKING ABOUT A SITUATION THAT'S UNLIKE OTHER PRODUCTS LIABILITY CASES WHERE THERE SOMETIMES IS A DISPUTE ABOUT WHETHER THE EVENT WAS POSSIBLY CAUSED BY A MEDICINE AND WHETHER, IN FACT, THE COMPANY KNEW ABOUT IT. THIS IS NOT ONE OF THOSE CASES. THE COMPANY WAS WELL AWARE OF THE RISK OF

DISCONTINUATION SYMPTOMS. AND KIND OF DOING A SIDE EXERCISE IN DISCOVERY ON PROZAC IS NOT GOING TO MATERIALLY ADVANCE WHAT WE CURRENTLY KNOW ABOUT THE COMPANY'S UNDERSTANDING OF THAT RISK.

THE COURT: ALL RIGHT.

OKAY. SO, WHAT I WOULD DO IS I APPRECIATE THE ARGUMENT. I UNDERSTAND WHAT YOU'RE SAYING. BUT FOR THE REASONS I HAD INDICATED EARLIER, I DO THINK THAT THE PLAINTIFF SHOULD BE ENTITLED TO GET INTO THAT ISSUE.

SO, I'M GOING TO ORDER THE PARTIES TO GO OUT AND MEET AND CONFER RIGHT NOW. SEE IF YOU CAN LIMIT THOSE REQUESTS FOR PRODUCTION. AND, PERHAPS, THERE'S A WAY OF DOING IT THAT WILL -- CAN, YOU KNOW, HELP LILLY TO DISCOVER APPROPRIATE DOCUMENTS WITHOUT PUTTING IN TOO MUCH -- TOO MUCH EFFORT.

AND THEN WITH RESPECT TO THE 30(B)(6), SEE WHAT YOU CAN FIGURE OUT WITH RESPECT TO THAT. IT'S JUST -- HAVING SOMEBODY TESTIFY AS TO THE NAMES OF PEOPLE INVOLVED IN SOMETHING THAT HAPPENED 20 YEARS AGO DOESN'T STRIKE ME AS A PARTICULARLY PRODUCTIVE WAY TO SPEND -- TO SPEND TIME.

SO, WHAT I'LL DO IS I'LL CALL THE MATTER AGAIN AFTER YOU'VE HAD AN OPPORTUNITY -- TAKE AS LONG AS YOU LIKE.

LET JAMES KNOW WHEN YOU'RE READY TO COME BACK. AND THEN I'LL HEAR FROM YOU AGAIN.

MS. JONES: UNDERSTOOD, YOUR HONOR. AND WE APPRECIATE IT.

ONE -- ONE POINT I JUST WANT TO MAKE --

THE COURT: YES.

MS. JONES: -- IS THAT I -- IT MAY BE NECESSARY FOR ME TO CONSULT WITH MY CLIENT ON SOME OF THESE MATTERS. SO, I'LL OBVIOUSLY TRY TO GIVE THE COURT AS MUCH GUIDANCE AS -- AS I CAN ON WHAT WE'RE PREPARED TO AGREE TO. BUT I JUST WANT TO OFFER THAT CAVEAT.

THE COURT: OKAY.

MR. LECKMAN: THANK YOU, YOUR HONOR.

THE COURT: ALL RIGHT. THANK YOU.

(RECESS AT 10:15 A.M. TO 10:57 A.M.)

MR. LECKMAN: GOOD MORNING, AGAIN, YOUR HONOR.

MATT LECKMAN HERE ON BEHALF OF THE PLAINTIFFS.

THE COURT: GOOD MORNING AGAIN.

MS. JONES: GOOD MORNING AGAIN, YOUR HONOR.

PHYLLIS JONES ON BEHALF OF ELI LILLY AND COMPANY.

THE COURT: GOOD MORNING AGAIN.

ALL RIGHT. SO, WHAT'S THE -- WHAT'S THE STORY?

MS. JONES: WELL, WE'VE MADE SOME PROGRESS. LET ME -- I'LL GIVE YOU JUST A RUN-DOWN ON WHERE I THINK WE ARE. AND, OBVIOUSLY, MR. LECKMAN WILL OFFER ANY THOUGHTS THAT HE HAS.

WE DID TAKE THE TIME THAT YOU HAD REQUESTED TO TALK ABOUT THE SPECIFIC REQUEST FOR PRODUCTION THAT ARE AT ISSUE HERE AS WELL AS THE 30(B)(6) NOTICE. AND I BELIEVE WE'VE REACHED AGREEMENT ON -- WITH RESPECT TO RFP 125, SOME

ALTERNATIVE LANGUAGE THAT FOCUSES THE REQUEST A BIT -- IN A BIT MORE DETAIL. AND I'M HAPPY TO SHARE THAT WITH THE COURT IF YOU'D LIKE TO, OR THE PARTIES CAN JUST PROCEED BASED ON THEIR AGREEMENT.

THE COURT: WELL, I THINK FOR THE RECORD IT WOULD BE WORTHWHILE TO GO AHEAD AND --

MS. JONES: OF COURSE.

AS I UNDERSTAND IT, THE REQUEST NUMBER 125 WILL BE REVISED TO SEEK ALL DOCUMENTS THAT CONTAIN THE WORDS "PROZAC, OPEN PAREN, FLUOXETINE, CLOSE PARENTHESIS, AND THE WORDS "WITHDRAWAL, DISCONTINUATION, DEPENDENCE, OR ADDICTION."

THE COURT: ALL RIGHT.

MS. JONES: THE OTHER AGREEMENT THAT WE'VE MADE WITH RESPECT TO RFP NUMBER 125 IS THAT I HAVE REPRESENTED TO MR. LECKMAN THAT I WOULD GO BACK TO MY CLIENT AND HAVE A CONVERSATION IN MORE DETAIL ABOUT KIND OF THE SOURCES OF DOCUMENTS RELATED TO PROZAC. BECAUSE THAT'S SOMETHING THAT I CURRENTLY DON'T HAVE A COMPLETE UNDERSTANDING OF AND WAS NOT ABLE TO REACH THE CLIENT WHEN I ATTEMPTED TO CALL A FEW MINUTES AGO.

BUT WE WILL COME BACK TO THE PLAINTIFFS WITH THE PROPOSAL ON THE SPECIFIC SOURCES OF DOCUMENTS THAT WE WOULD PROPOSE TO SEARCH TO IDENTIFY THE DOCUMENTS SOUGHT UNDER THE REVISED VERSION OF RFP 125.

THE COURT: ALL RIGHT.

MS. JONES: AS I UNDERSTAND IT, ON REQUEST NUMBER 140, THE LANGUAGE WILL REMAIN LARGELY AS WRITTEN. ALTHOUGH, OUR AGREEMENT AT THIS POINT IS THAT I WOULD GO BACK TO THE CLIENT. AND WE WILL EXPLORE WHETHER OR NOT THE COMPANY HAS A LISTING OF ANY ARTICLES THAT WERE SPONSORED OR -- SPONSORED BY LILLY OR ON WHICH LILLY CONSULTED ON ITS OWN OR THROUGH A THIRD PARTY WITH RESPECT TO WITHDRAWAL, DISCONTINUATION, DEPENDENCE OR ADDICTION RELATED TO PROZAC OR FLUOXETINE.

AS I UNDERSTAND IT, WE ALSO HAVE AN AGREEMENT THAT LILLY WILL NOT BE PRODUCING THE FINAL PUBLISHED VERSIONS OF DOCUMENTS THAT ARE AVAILABLE THROUGH THE PUBLIC DOMAIN.

THE COURT: ALL RIGHT.

MS. JONES: AS TO RFP NUMBER 141, WE'VE AGREED THAT I WOULD GO BACK TO THE CLIENT AND HAVE A DISCUSSION ABOUT WHETHER OR NOT THERE IS SOME CENTRAL REPOSITORY OR LISTING THAT DETAILS ALL THE CME PRESENTATIONS THAT WERE SPONSORED BY THE COMPANY AND EXPLORE WHETHER THERE ARE, IN FACT, ANY WRITTEN MATERIALS RELATED TO CME PRESENTATIONS THAT WERE CONDUCTED ON THE SUBJECT OF PROZAC, FLUOXETINE AND DISCONTINUATION, DEPENDENCE, ADDICTION OR WITHDRAWAL.

THE COURT: ALL RIGHT.

MS. JONES: SO, I BELIEVE THAT'S OUR UNDERSTANDING WITH RESPECT TO THE RFP'S. AND THAT COVERS THAT FIRST BUCKET OF PROZAC DISCOVERY THAT HAD BEEN SOUGHT.

WITH RESPECT TO THE RESEARCH SYMPOSIUM 30(B)(6)

NOTICE, AS I UNDERSTAND MR. LECKMAN'S POSITION, HE IS PREPARED TO FOREGO THE SIX TOPICS THAT ARE LISTED IN THAT 30(B)(6) NOTICE BUT WOULD LIKE TO MAINTAIN ONE OF THE TWO DOCUMENT REQUESTS WHICH CURRENTLY SEEKS ANY AND ALL DOCUMENTS, MATERIALS AND THINGS RELATING TO THE SYMPOSIUM, INCLUDING, BUT NOT LIMITED TO, AUDIO OR VIDEO RECORDINGS OF ANY PART OF THE SYMPOSIUM.

WHAT I HAVE TOLD MR. LECKMAN IS THAT I'D BE HAPPY TO GO BACK AND SPEAK WITH THE CLIENT ABOUT THE EXTENT TO WHICH ANY SUCH RESPONSIVE MATERIALS MIGHT EXIST SUBJECT TO THE UNDERSTANDING THAT WE MAY HAVE AN OBJECTION ON THE GROUNDS THAT THAT REQUEST REMAINS OVERBROAD OR UNDULY BURDENSOME. BUT FOR THE TIME BEING, WE'RE HAPPY TO GO BACK AND LOOK AND SEE WHAT ACTUALLY EXISTS WITH RESPECT TO THAT DOCUMENT REQUEST.

THE COURT: ALL RIGHT.

MS. JONES: MR. LECKMAN WILL OBVIOUSLY CORRECT ME IF I'VE GOTTEN ANY OF THAT WRONG, BUT I BELIEVE THAT FAIRLY REPRESENTS OUR UNDERSTANDING AT THIS POINT.

THANK YOU, YOUR HONOR.

THE COURT: OKAY. THANK YOU.

MR. LECKMAN: THANK YOU, YOUR HONOR. MATT LECKMAN FOR THE PLAINTIFFS.

JUST -- SO, COUNSEL IS CORRECT IN HER STATEMENTS TO THE COURT RELATING TO OUR MEET AND CONFER ON THOSE SEVERAL TOPICS. JUST A COUPLE OF ADDITIONAL COMMENTS TO AUGMENT THE

DISCUSSION AND HELP THE COURT HAVE AN UNDERSTANDING OF WHERE WE'D NARROW THE BREADTH.

WITH RESPECT TO REQUEST NUMBER 140, WHICH DEALS WITH CERTAIN -- WHICH DEALS WITH THE REQUEST FOR ARTICLES AND ITEMS THAT LILLY MAY HAVE PARTICIPATED IN, AS I EXPLAINED TO COUNSEL -- AND I WANT THE COURT TO UNDERSTAND -- I CERTAINLY DO NOT WANT LILLY TO HAND ME WHAT'S ALREADY IN THE PUBLIC DOMAIN. I UNDERSTAND THAT THAT WOULD BE A SILLY EXERCISE.

WHAT I AM LOOKING FOR AND WHAT I EXPLAINED TO COUNSEL IS THAT IN MY EXPERIENCE PHARMACEUTICAL COMPANIES HAVE -- OFTEN HAVE A PRACTICE OF RETAINING OUTSIDE VENDORS TO ASSIST IN CONSULTING AND HELPING TO CREATE MEDICAL LITERATURE THAT SUPPORTS THEIR PRODUCTS. IT'S NOT AN ILLEGAL PROCESS, BUT IT IS SOMETHING COMMONLY REFERRED TO AS "GHOST WRITING." IT'S WHERE THEY HAVE A THIRD-PARTY VENDOR COME IN AND ASSIST ON PREPARING A PAPER THAT EVENTUALLY BECOMES PEER REVIEWED AND IS USUALLY FAVORABLE TO THE PRODUCT.

I'M INTERESTED IN THAT REALM. I'M INTERESTED IN WHERE LILLY MIGHT HAVE DONE THAT IF THEY DID THAT WITH RESPECT TO PROZAC AND WITHDRAWAL. AND, SO, I DON'T WANT THINGS THAT ARE IN THE PUBLIC DOMAIN. I DON'T WANT FINAL PUBLISHED PAPERS, BUT I WANT TO SEE THE BACK STORY TO ANY GHOST WRITING OR PREPARATION OF ARTICLES THAT EVENTUALLY WERE PUBLISHED WITH LILLY'S DIRECT ASSISTANCE OR THROUGH -- THROUGH A THIRD PARTY.

SO, I DID NOT WORD THE REQUEST VERY WELL THE FIRST

TIME AROUND. AND WE HAVEN'T PENNED IT TO PUT A FINER POINT ON IT, BUT THAT'S WHAT I EXPRESSED TO COUNSEL. AND THAT'S ESSENTIALLY WHAT WE'RE LOOKING FOR WITH THAT REQUEST.

WITH RESPECT TO 141, I CERTAINLY -- COUNSEL MADE THE FAIR POINT WITH RESPECT TO, YOU KNOW, THINGS THAT MIGHT HAVE BEEN UTTERED AT CONTINUING MEDICAL EDUCATION PRESENTATIONS OVER THE COURSE OF THE LAST 20 YEARS. LILLY WOULD HAVE NO WAY TO KNOW WHAT ANY PRESENTER MIGHT HAVE SAID IN A CROWD OF A HUNDRED PEOPLE.

WHAT I'M SIMPLY LOOKING FOR IS IF THERE ARE DOCUMENTS AND THINGS THAT WERE MEMORIALIZED OR SAVED, WERE CREATED FOR THE PURPOSE OF PRESENTING OVER THE YEARS WITH RESPECT TO PROZAC AND WITHDRAWAL THAT LILLY IS IN POSSESSION OF, THEN, I'D LIKE THOSE WRITTEN MATERIALS.

WITH RESPECT TO THE SYMPOSIUM, THE '97 SYMPOSIUM, I KNOW YOUR HONOR'S SUGGESTION WAS THAT WE REDUCE THOSE REQUESTS TO INTERROGATORIES.

I THOUGHT THE EASIER THING TO DO MIGHT JUST BE TO SIMPLY GO WITH THE DOCUMENT REQUEST, THE SINGULAR ONE THAT ASKS FOR MATERIALS RELATING TO THAT SYMPOSIUM AT THE END.

COUNSEL HAS INDICATED INITIALLY THAT THEY MAY TAKE A POSITION THAT THAT'S OVERBROAD OR UNDULY BURDENSOME -- BURDENSOME. OBVIOUSLY, WE DISAGREE. I THINK IT'S A NARROW -- IT'S ONE EVENT IN TIME. I'M NOT ASKING FOR SYMPOSIA OVER THE YEARS, MULTIPLE SYMPOSIA. SO, I DON'T KNOW THAT WE NEED TO

HASH THAT OUT TODAY, BUT THAT'S OUR POSITION. AND I EXPECT THEM TO GET BACK TO ME FROM THEIR CLIENT ON THAT.

SO, I THANK YOU, YOUR HONOR. AND UNLESS YOUR HONOR HAS ANY FURTHER QUESTIONS, I THINK THAT'S AN ACCURATE REFLECTION OF OUR MEET AND CONFER.

THE COURT: ALL RIGHT. THANK YOU.

SO, IS THERE ANYTHING FURTHER?

MS. JONES: NO, YOUR HONOR.

THANK YOU VERY MUCH.

THE COURT: ALL RIGHT. THANK YOU.

THE CLERK: COURT IS NOW ADJOURNED.

(PROCEEDINGS ADJOURNED AT 11:05 A.M.)

C E R T I F I C A T E

I CERTIFY THAT THE FOREGOING IS A CORRECT TRANSCRIPT FROM THE ELECTRONIC SOUND RECORDING OF THE PROCEEDINGS IN THE ABOVE-ENTITLED MATTER.

/S/ DOROTHY BABYKIN 9/17/14

FEDERALLY CERTIFIED TRANSCRIBER DATED

DOROTHY BABYKIN

EXHIBIT 21

BRINTNALL & NICOLINI, INC.
HEALTHCARE CONSULTING AND RESEARCH

Prozac
Pyramid™ Positioning/
Message Development Research

Prepared for

Eli Lilly

June 2000

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EXECUTIVE SUMMARY

Eli Lilly and Company (Lilly) contracted with Brintnall and Nicolini, Inc. (B&N) to utilize its Pyramid Positioning/Message Development™ process to reposition Prozac with four physician segments: psychiatrists and primary care physicians (Faders, Undecideds, and Enthusiasts). B&N conducted the work during February/March 2000. The Pyramid process had two work phases. The first phase was developmental and involved marketing management, medical and the advertising agency of record. This expert team sought to develop a more-effective Prozac selling story and positioning as they listened to 20 interviews with a national sample of physicians, including 12 primary care physicians (PCPs) and 8 psychiatrists (PSYCHs) recruited from Lilly's lists. The team debriefed and revised the Prozac selling story between interviews. The second phase of the Pyramid process involved qualitative testing of two developed messages, one for PCPs and the other for PSYCHs. This phase consisted of 25 phone interviews divided among the aforementioned segments. Subsequent to the testing work, B&N conducted another 11 interviews divided about equally between PCPs and PSYCHs, to evaluate refined versions of the same developed messages as well as an alternate PCP message introducing the new idea of Prozac providing "short-term power and long-term protection."

- The developmental process yielded an umbrella Prozac positioning of "power and versatility", which applies across the four segments. The PCP and PSYCH developed messages have similar structures organized around patient types, but the reasons to believe the patient types themselves diverge slightly.
  - For PCPs, power resides in the ability of Prozac to energize depressed, unmotivated patients, and its versatility is in its proven ability to treat specific patient types, including female patients and the elderly. An early version of the PCP message mentions the "dual efficacy of fluoxetine" (due to its potent norfluoxetine metabolite), using this reference as another means of conveying "power." However, this statement was dropped midway through the testing phase.
  - For PSYCHs, the power of Prozac is the ability of Prozac to treat "complex and challenging" patients effectively, including partial and non-responders, and its versatility in its effectiveness and safety in treating female patients and elderly patients with comorbidities. The developed PSYCH message refers to Prozac's effect on other monoamines beyond serotonin.
- Overall, both the PCP and PSYCH developed messages proved effective in stimulating physicians who prescribe less Prozac to consider prescribing Prozac more often, because the messages remind physicians that Prozac is a powerful antidepressant and has long been considered the gold standard for efficacy.

- After reading the message, almost all of the Faders and about half of the Undecideds are inclined to use more Prozac, particularly for women and the elderly. Prozac Faders anticipate the largest increase in usage. This increased usage is predominantly at the expense of Paxil, Zoloft, and Serzone. In general, physicians claim that they already often prefer Prozac in low-energy patients; therefore, they do not anticipate much increase in use for this group.

- Prozac Enthusiasts, in contrast, are less responsive to the message because they feel that it merely confirms their reasons for already preferring Prozac for many patients.

- Similarly, PSYCHs can be divided into two categories: those who are currently prescribing less Prozac and those prescribing more. The lower Prozac prescribers, who are often high users of Zoloft, respond that they will increase Prozac use in elderly patients and women, primarily at the expense of Celexa and Zoloft. In addition, a few say that they would substitute Prozac for Effexor in some instances, because of Prozac's high success rate, 40-mg dosage strength, and better tolerability profile.

♦ The PCP message is compelling because many PCPs find the information new and significant, particularly the fact that Prozac is

  - Safe in renally-insufficient patients, often elderly

  - Safe in pregnancy

  - Effective in relieving even the physical symptoms of PMDD

  - FDA-approved for use in PMDD, bulimia, and the elderly

  - Available in a variety of dosage formulations, including a 40mg dosage-form for patients requiring a higher dose, and a liquid formulation for nursing-home patients

♦ The PSYCH message is also compelling because of new and important information, particularly the facts that

  - Prozac works in Zoloft non-responders

  - Patients stay on Prozac longer than on other SSRIs

  - Prozac is effective even for the physical symptoms of PMDD

  - Prozac does not accumulate

- Importantly, after reading the developed message, PCPs and PSYCHs agree that "powerful and versatile" aptly describes Prozac and supports their clinical experience. Physicians readily accept that Prozac can effectively energize depressed patients, since this confirms their perception of Prozac as an activating antidepressant.
  - Removing the dual-acting metabolite information from the PCP message during the second half of the testing interviews seemingly did not affect PCPs' perception of the power of Prozac but it did address their confusion and disinterest.
  - Replacing power and versatility with "short-term power and long-term protection" in an alternate PCP message tested only with six PCPs, also appears to lead to more questions about Prozac's power. In this alternative message, PCPs expressed confusion about the meaning of "short-term power" and they rejected the claim that Prozac does not require titration.
- The key reasons why physicians do not prescribe even more Prozac in response to the developed messages are:
  - Inappropriateness of Prozac for patients who are anxious-depressed or who require sedation
  - Cost and lack of reimbursement for patients who must pay out of pocket
  - Patient reluctance due to Prozac's perceived side effects, such as loss of libido, violent behavior, and suicidal tendencies
  - Comorbidities such as smoking or ADHD, which may lead physicians to favor the use of other antidepressants
- Importantly, physicians often comment that they expect to use the information in the messages to help overcome the barrier of patient reluctance, but expect that some patients will simply not accept a Prozac prescription.
- Several points in the developed messages generate recurring disinterest, confusion, and skepticism:
  - PSYCHs seem uninterested in the listing of complex and challenging patient types at the beginning of the message. Accordingly, it may be better to start with the idea of "in your hands, Prozac can be a powerful and versatile tool" and then move to the patient types.
  - The Zoloft non-responder claim in the PSYCH message raises questions about doses used in the study and whether Zoloft may also be as effective with Prozac non-responders.

- Similarly, both PCPs and PSYCHs ask for more details about the study, showing that patients stay on Prozac longer than on Zoloft, Paxil, and Celexa.

- Across segments, the idea that Prozac does not accumulate is attractive. Nonetheless, physicians find this claim counterintuitive because of Prozac's long half-life. Prozac sales representatives should be prepared to deal with this potential source of confusion.

- Most PSYCHs comment that it has been their impression that Prozac is metabolized by the cytochrome P450 system in the liver, rendering it potentially problematic in patients on multiple medications, as is typical of the elderly.

- Both PCPs and PSYCHs take away and reject the implication that fatigue and lack of motivation are particularly characteristic of female patients. This suggests a need to fine-tune the connections among patient types in the messages.

Recommendations

Based on the findings from the validation phase of research, Eli Lilly should consider making the following changes to the Prozac messages.

Common to Both Messages

- Consider clarifying the idea that fatigue and lack of motivation are not exclusive to females.

- Consider expanding on the idea that Prozac's long half-life prevents discontinuation syndrome, making direct comparisons to Paxil and Zoloft.

- Explain why Prozac does not accumulate despite its long half-life.

- Possibly combine the sub-bullets under "the most studied in patients with concurrent medical conditions" statement, as physicians ignore the "effective at relieving depression" statement.

- Consider creating a separate headline for the dosage-form information, as may be leveraged more effectively to convey the idea of versatility.

- Consider changing the "10 mg in the elderly statement" to 5 mg, as many physicians state that the 10 mg can be broken in half.

Specific to PCP Message

- Consider rewording the "power and versatility" statement to avoid MDs misconstruing this idea to mean singling females out as having symptoms of fatigue and lack of motivation.
- Consider expressing vague aches and pains by using the words "somatic complaints," as this language seems to mimic physicians' own.
- Consider removing the assertion that Prozac shows efficacy in one week.

Specific to PSYCH Message

- Similar to the PCP message, consider making the opening line more dynamic and attention-grabbing, raising their interest to hear more. Possibly incorporate the fact that new data are available.
- Re-contextualize the phrase "prescription claims studies" so that PSYCHs quickly identify where these data come from, elevating the credibility of this statement.
- If possible, make the Zoloft non-responder data more credible by adding a reference to the study.

OBJECTIVES AND METHODOLOGY

As Prozac (fluoxetine) enters the mature phase of the product lifecycle, it is facing increasing competition as well as the challenges associated with losing patent protection. Hence, Eli Lilly is developing new marketing strategies and tactics intended to protect the brand's share of the antidepressant market during its maturity. To this end, Eli Lilly and Co. contracted with Brintnall & Nicolini, Inc. (B&N) to utilize its proprietary message development process to reposition and develop new selling messages for Prozac. The results from this strategy-development work serve as a communication platform for subsequent tactical campaign elements. Eli Lilly and B&N conducted the work during February/March, 2000.

The specific objectives of the study were to:

- Develop a compelling Prozac positioning designed to be unique, credible, important and behavior-modifying (motivates physician to prescribe)
- Develop a Prozac positioning statement
- Create a product message to communicate the positioning immediately and powerfully
- As appropriate, modify the core communication for different Prozac customer segments
- Uncover how physicians position Prozac vis-a-vis their other therapeutic options
- Provide a qualitative validation of the product messages and some message variations by measuring consistency of response

The Message Development technique is a creative yet rigorous process utilized to develop a powerful selling message and an appropriate positioning statement. The process has three steps: 1) a Strategy Session, 2) Message Transformations, and 3) Message Testing. The next sections describe each of the steps in detail.

Strategy Session. The purpose of the Strategy Session is for B&N to inform the team about the nature of the Message Development process. In addition, the team shares information and insights about the market and reviews motivational goals for the selling messages. Finally, the team reaches agreement on the appropriate starting message to use at the beginning of the transformational process. The Strategy Session for this project was held on the morning of February 14, 2000.

Message Transformations. The transformational work is a creative process in which an expert team develops a compelling message by observing and responding to the reactions of target physicians as seen during in-depth interviews using trial messages. After each transformational interview, there is a thorough debriefing, which identifies barriers and discusses ways to overcome those barriers. The team then agrees on what changes, if any, to make to the selling messages and makes the changes. Following those modifications, the team then introduces the revised message into the next interview. For this research, the team interviewed a sample of eight (8) psychiatrists (PSYCHs) and twelve (12) primary care physicians from three market segments: 6 faders, 3 undecided and 3 enthusiasts, (see the Appendices for the Screening Questionnaire), for a total of 20 interviews. The physicians were about evenly divided across five cities: Philadelphia, Charlotte, Chicago, Denver and Seattle. B&N recruited physicians from lists provided by Eli Lilly. These videoconference and face-to-face interviews took place at the B&N videoconference facility in Philadelphia from February 14 through 18, 2000.

The Message Development interviews are deliberately non-directive and conversational. Physicians initially describe the general nature of their practices. A customized pre-message-exposure exercise follows: physicians estimate the percentage of patients for whom they prescribe various products listed on an allocation grid. After explaining their estimates, physicians review the product message and share their reactions. Then they reallocate their prescriptions and explain any changes. (See Appendices for the Discussion Guide and the Product Allocation Grid.)

Message Testing. The next phase of the Message Development process evaluates the developed messages through a series of in-depth interviews intended to gauge their communicational validity and motivational impact. (See the Appendices for the Developed Messages.) These interviews permit B&N to suggest areas of needed refinement in the developed messages. B&N conducted 25 telephone-depth validation interviews among 8 PSYCHs and 17 PCPs (5 faders, 6 undecided and 6 enthusiasts), for a total of 25 interviews. These interviews were completed on February 24, 2000. During this process, a total of 2 developed messages for PCPs and 1 developed message for PSYCHs were tested. These physicians were also recruited from lists provided by Lilly. All physician participants received appropriate honoraria to encourage participation.

After the initial phase of Testing interviews, B&N conducted an additional 11 interviews with five (5) PSYCHs and six (6) PCPs (both FPs and IMs) to evaluate refined versions of the developed messages as well as an alternative PCP message introducing the new idea of Prozac providing "short-term power and long-term protection." These interviews were completed on March 10, 2000.

Overview of Sample. The full message development process included a total of 56 physician interviews, as summarized in the following table:

Specialty	Development	Testing	Additional Testing	Total
PCPs				
	12			
	17			
	6			
	35			
PSYCH				
	8			
	8			

	5
	21
TOTAL	
	20
	25
	11
	56

B&N audio-recorded the interviews for subsequent analysis. Copies of these tapes, if not already provided, accompany this final report.[1]

The next section of this report contains the Detailed Findings, followed by the Appendices. Keep in mind that the transformational work phase of Message Development is not simply market research, but rather is a facilitation process that enables an expert team to respond creatively to insights based on customer listening. The validation phase of Message Development is similar to qualitative market research. Finally, the nature of the entire Message Development research process, as well as this resultant report, are proprietary B&N material subject to a mutual understanding of confidentiality between Lilly and B&N. This understanding prohibits any use or direct/indirect disclosure of B&N's proprietary research techniques or reports to competitors.

[1] According to our covenant with the participants, duplication or distribution of, or quotation from, any interview tapes without the express written permission of B&N is strictly prohibited.

DETAILED FINDINGS

CONTEXT

PCPs report increasing levels of autonomy in the treatment of mild-to-moderate depression.

PCPs consistently report that the treatment of depression is a growing segment of their practices. Since the advent of the SSRIs, PCPs say that they have developed a greater comfort level and are able to treat the vast majority of mild-to-moderate depression successfully without the help of PSYCHs. Almost all PCPs indicate that they refer patients to PSYCHs after the first visit only when patients present with suicidal or homicidal ideations, symptoms of psychosis, or other concomitant psychological disorders that may cloud the diagnosis. PCPs say they also refer patients out to PSYCHs after an inadequate trial of one or two SSRIs.

> *I think with the advent of the newer medications that have fewer adverse effects, we are being more liberal in treatment with medications. I am also thinking more now of the many associated medical or psychological disorders that are associated with depression, such as anxiety and obsessive/compulsive disorders. We are more tuned in to these associated illnesses since these medications have indications for those disorders as well. (PCP-Enthusiast)*

> *I'll use one or perhaps two different types of medications to see if it will help, and if I kind of hit the wall, then I will refer them over to a PSYCH, more for medication management. (PCP-Fader)*

Interestingly, many PCPs also report a reluctance to refer patients into managed care behavioral health systems, due to concern over patients' willingness to navigate through these sometimes complicated systems. Some PCPs even express concern over the quality of care their patients will receive within managed behavioral health systems. This reluctance to refer patients appears to be particularly evident when a trusting relationship between the PCP and patient has already been established. PCPs also report that higher levels of public awareness of depression combined with lower levels of social stigma drive an increasing number of patients into their offices seeking treatment. These are some of the factors that result in PCPs treating depression more often and more aggressively than in the past.

The HMOs' plan is to keep them out of the PSYCHs offices by demanding a psychology referral first, so the patients go into the behavioral health network and get lost in that maze for a while before they get the appropriate referral. So I tell my patients that this is not something I cannot manage for them and often involve them in the decision to see a PSYCH. (PCP-Fader)

Focusing almost exclusively on complex and often difficult-to-treat patients, PSYCHs are employing more sophisticated pharmaceutical regimens than in the past.

PSYCHs report that the use of polypharmacy has become far more prevalent in treating depression, combining agents that address different neurotransmitters. In fact, some PSYCHs say that the majority of their patients are currently taking more than one antidepressant. The reasons behind this new approach stems, in part, from the increased appreciation of the biochemical basis of depression and the recognition that multiple neurotransmitters may play crucial roles. For instance, they may augment SSRI therapy with Wellbutrin because it has an effect on a different neurotransmitter. Polypharmacy also allows them to mitigate side effects by permitting lower doses of each agent.

For me, there is more emphasis on multi-pharmacy where it's appropriate. Mixing various classes of drugs to achieve augmentation strategies or certain goals…more experimentation when I run out of easy solutions and there don't seem to be any other immediate available ones. (PSYCH)

As a third-line option, I may combine an SSRI with Wellbutrin to achieve an enhanced antidepressant effect. (PSYCH)

I think that some patients need a noradrenergic or dopaminergic component to their treatment where the re-uptake is more available. This is when I might choose a drug like Effexor or Wellbutrin. (PSYCH)

While they do not indicate major differences in overall efficacy among SSRIs, both PSYCHs and PCPs consider Prozac to be among the most powerful.

Physicians across specialties acknowledge the fact that Prozac is the oldest SSRI; however, they consistently indicate a high comfort level with the product and a perception that Prozac is still considered to be among the quickest to show efficacy and possibly the most potent overall. In addition, these physicians recognize Prozac as having a wide range of indications. Some physicians even assert that Prozac is the gold standard against which all others are compared. However, physicians across specialties report that efficacy alone does not strongly differentiate the SSRIs. They say that side effects more clearly differentiate these products, and that side-effect profiles more often guide their choice of SSRI. For example, Prozac, with its energizing effect, is often used for patients who need a lift. In contrast, Paxil seems the more popular choice for patients who have an anxiety component to their depression.

> *It's the drug I have most experience with and I have a feeling it is perhaps the most potent, and perhaps … shows effectiveness early on. I think it (Prozac) has the indications for most of the conditions that I've mentioned. And I kind of think of it as restoring more functional patients, back to more normal function more quickly. (PCP – Enthusiast)*

> *Prozac was the first SSRI and actually is one of the best. It went into eclipse a little bit when a lot of competition came out, but it's still…when you look at all the new drugs that came out, have they eclipsed Prozac's efficacy? And the answer is by and large no. As a general picture, Prozac is still one of the most powerful, potent and efficacious SSRIs and it has a long history of being such. (PSYCH)*

> *Paxil ... I have again a perception of it perhaps being a little bit more calming, more sedating for patients with a lot of anxiety, and it has indications for panic disorder. I tend to use it for individuals with depression plus a lot of agitation and anxiety. (PCP – Enthusiast)*

Prozac is primarily prescribed to patients who will benefit from its activating properties without being bothered by untoward effects.

PSYCHs report that most patients who receive Prozac need its activating properties. They often refer to Prozac patients as those with retarded depression. However, a significant number of physicians claim to add trazodone occasionally, when their patients report what they perceive to be Prozac–induced insomnia. Physicians also choose Prozac for patients whom they consider to be non-compliant with medications, due to its long half-life.

> *It tends to energize patients a little bit more than the others do. (PCP – Fader)*

> *Patients that have problems with compliance – the long and lasting effect is good for the non-compliant ones. (PSYCH)*

> *Once-a-day dosing and a lot of experience with it. It doesn't matter much if people miss a dose here or there because of the long half-life. It has brand-name recognition and is neutral on weight. I will use it on any depressed patient, maybe one who is familiar with it, or one who has a lot of trouble taking medications, so the once-a-day dose is important to them. (PSYCH)*

Concern about side effects (especially sexual dysfunction); potential to exacerbate anxiety in more anxious-depressed patients; and drug interactions are the most commonly mentioned reasons for avoiding Prozac. In addition, some physicians claim that some patients refuse Prozac based upon negative perceptions read in the lay press. Among GPs, high cost is also occasionally mentioned as a barrier to use. As a result, a significant number of physicians claim they have been prescribing less Prozac in recent years and more of the newer atypical antidepressants.

> *I try to stay away from Prozac in my younger male patients because of sexual dysfunction. (PSYCH)*

> *I do worry about the P450 interactions in my elderly population. I have started trying some of the other agents in an attempt to avoid that. (PSYCH)*

The negative thing is that some patients are conditioned to not like to use it…they've heard bad press…And they also aren't familiar with it and they feel embarrassed if their friends and relatives were to know that they were on Prozac. They would associate it with perhaps major mental disease. I've had mothers call back and insist that I remove any record from the chart of the patient who they thought was put on Prozac. So some people are fairly emotional about the drug in a negative way. (PCP – Enthusiast)

I use Prozac but I have trouble with patients who say you know…Oh Prozac, I have heard about that. My neighbor had it and died on it. There are still those stories that float around about Prozac. I don't believe them and I take the time to tell patients that they're false. But if a patient comes into my office and says: 'I am not going to take it: that drug killed my uncle', I am just wasting my time trying to convince them. So I don't try to do that anymore. (PCP – Fader)

Most PCPs and PSYCHs are still gaining experience with Celexa, the newest SSRI.

Although Celexa is relatively new to the physicians' armamentarium, common favorable perceptions of Celexa are that it has fewer side effects than the other SSRIs (especially in terms of sexual dysfunction); is less expensive; is included on many formularies; has a favorable drug-drug interaction profile; and comes in scored tablets.

I think of it as perhaps having fewer drug interactions. The pharmaceutical representatives tend to use that sales pitch a lot…so I tend to use that with patients who have multiple medications. (PCP – Enthusiast)

It's pretty new. I'm starting to use it through one plan that has it as the only SSRI, and I've been detailed on it…it looks pretty clean. (PCP – Fader)

One, it's on everybody's formulary right now. Two, it's less expensive if they're not on formulary. Three, it seems to work quite well with fewer side effects. (PCP – Fader)

However, it appears that some physicians are still questioning whether Celexa is truly an improvement over the other SSRIs. For example, a few comment that Celexa may not provide long-term efficacy as well as the other SSRIs, while a few others say that they are witnessing sexual dysfunction with Celexa at rates higher than the company is promoting.

Celexa, I tried when it first came out. It seems to be very well tolerated. Efficacy seems to be the question mark there. I haven't seen overwhelmingly positive results from the feedback I've been getting. (PCP – Undecided)

In the Medical Letter, when they give the introductory piece on Celexa, they mention that out of five double-blind studies, in something like two of them it was no better than placebo. The fact that it has been bounced around in Europe and took so long to come over here makes me wonder why, and then I see about studies: substantial number of the studies showing no better than placebo makes me wonder about the efficacy. (PCP – Fader)

It has a lot of sexual dysfunction. This is false advertising with Celexa, in my opinion, at least false rumors about it. So I've been turned off a bit. Patients have it, and my recollection is I originally got a lot of information saying it wouldn't have any sexual dysfunction. Then I found people had it. So I distanced myself a bit. (PSYCH)

MDs most often use Paxil in depressed patients with symptoms of anxiety; however, its associated fatigue and discontinuation syndrome is sometimes cause for concern.

Because of Paxil's perceived calming side effect, physicians often use it for patients who have significant symptoms of anxiety or insomnia associated with their depression. A significant number of MDs mention the manufacturer's marketing efforts touting its efficacy in social phobia. In addition, the PSYCHs, in particular, generally perceive Paxil as having a wide range of FDA-approved indications. However, few seem to be able to list them. Commonly-perceived drawbacks of Paxil include weight gain, increased fatigue, and withdrawal symptoms upon discontinuation.

I give Paxil to depressed patients, with some mild insomnia, mild agitation. (PSYCH)

If they had insomnia, I wouldn't worry about (Paxil) creating a problem. So I would use it more comfortably in somebody who had insomnia, because I knew I wouldn't be making it any worse. The patient who had some anxiety component along with their depression, I think I'd get a little better result. (PCP – Fader)

Paxil…the positive things about this…I have again the perception of it perhaps being a little bit more calming, more sedating for patients with a lot of anxiety and it has indications for panic disorder. I tend to use it for individuals with depression plus a lot of agitation and anxiety. (PCP – Enthusiast)

PCPs and PSYCHs say they consider Zoloft to be an intermediate product well-suited for the elderly.

Physicians perceive Zoloft to have a slightly milder energizing side-effect profile than Prozac and to be less sedating than Paxil. In fact, these physicians say they often substitute Zoloft for Prozac if patients resist taking Prozac. Some physicians choose Zoloft as their first-line agent for the elderly, because it is not metabolized by the cytochrome P450 system. In addition, many physicians like Zoloft because the 100 mg scored tablet can be broken in two, saving on expense.

> *It's pretty much the same profile as Prozac. Any depressed patient…no particular reason to use it. Maybe if someone has tried Prozac and doesn't like it or they had experience with Zoloft before, doesn't want to be sedated. (PSYCH)*

> *I use that more in elderly patients. I start them out on the low dose. I'm comfortable with the side-effect profile. It seems to work for them. (PCP – Fader)*

> *I'm largely geriatric practice and the short half-life is a little attractive there because of the fact that if you get into trouble, you can get out of trouble faster. Another thing that favors the Zoloft use in our HMO, it is preferred. They tell us to put people on 100 mg and split the pills in two so they can save some money. Virtually all the HMO patients I'll put on, if I put them on an antidepressant, they'll be on Zoloft. Also, it has a little more favorable interaction profile than Prozac. (PCP – Fader)*

MDs across specialties consider Effexor to be more efficacious than the SSRIs, attributing its greater efficacy to its effect on the norepinephrine system.

Currently, Effexor is most often relied upon after one or more SSRIs fail. However, it seems that a growing number of PSYCHs are using it first-line as well. The majority of these physicians attribute Effexor's greater efficacy to its effect on the norepinephrine system. PSYCHs, in particular, report increased use of Effexor since the sustained release formulation was made available. In addition, a significant number of PSYCHs and PCPs cite Effexor's efficacy in treating depression with a prominent anxiety component. Anxiety, they say, is a main theme of the manufacturer's sales pitch. A few PSYCHs report the need to start Effexor at low doses (most often 75mg) and titrate upward to avoid causing nausea.

I use Effexor for depressed patients maybe with some anxiety, as a prominent component of their depression. I tend to think of it more likely for someone who maybe was on other antidepressants or is somewhat treatment-resistant. (PSYCH)

I do use Effexor, but usually after failure with other drugs. (PCP – Enthusiast)

Effexor is used in patients who have anxiety with depression. That seems to help there well. Especially in women, it seems to work quite well. (PCP – Fader)

Effexor makes claims of affecting norepinephrine, and we see higher response rates with that medication. (PSYCH)

PSYCHs, in particular, often use Wellbutrin as second-line to Prozac for its energizing properties and lack of sexual dysfunction and in augmentation strategies with SSRIs.

Besides its use in helping people to quit smoking, Wellbutrin is often used as an "activating" antidepressant, replacing Prozac for tired/fatigued patients who are experiencing sexual dysfunction either as a result of their depression or as a side effect from an SSRI. In addition, PSYCHs say that they are using Wellbutrin for OCD and in combination with an SSRI for patients with refractory depression.

I use Wellbutrin for a depressed patient who is sluggish and sleeping a lot. (PSYCH)

I use that for individuals that may have sexual dysfunction problems to begin with. (PSYCH)

I use Wellbutrin with people who may be smoking and who tend to have a lot of fatigue; younger patients who definitely don't want sexual dysfunction, because they have trouble with that already. (PCP – Fader)

INSIGHTS FROM THE TRANSFORMATIONS

The following section outlines what message transformations were made during the developmental process and provides the supporting rationale for making each change to the messages.

Among primary care physicians, but particularly among psychiatrists, the overwhelming majority perceive themselves as individualizing their choice of antidepressant therapy. Therefore, they rejected the early versions of the messages, which were symptom-oriented, and perceived as promoting Prozac for all depressed patients. The listing of symptoms, such as "tired all the time, unmotivated, having difficulty concentrating, vague aches and pains, overwhelmed by work and family commitments" and even the idea of "re-energizing depressed patients" contributed to this impression of generic depression. Therefore, the developed messages took on a patient-type orientation, reducing the number of symptoms mentioned.

The PCP and PSYCH messages diverged in their patient types. For PCPs the types were 1) the low-energy, 2) the female, and 3) the elderly. For psychiatrists, the low-energy patient type was replaced by the partial or non-responder requiring a more effective treatment. Psychiatrists expressed more interest in the ability of Prozac to handle these more difficult patients and in the concept of other neurotransmitters (norepinephrine) becoming affected at higher doses. In contrast, primary care physicians disliked the idea of needing to titrate an antidepressant, pointing out the cost implications of increasing the dose. Therefore, the PCP message emphasized Prozac's start-with-stay-with efficacy claims.

- In an attempt to maintain PCPs perception of Prozac's power, information was added regarding Prozac's unique dual efficacy stemming from a combination of fluoxetine and its metabolite norfluoxetine. However, PCPs found this information confusing and the team decided to drop it during the refinement phase of research.

The developed Prozac messages are significantly longer than in their initial form: the idea of addressing the needs only of patients requiring more energy or of partial/non-responders tended to confirm current use of Prozac rather than to expand usage. Therefore, both developed messages add two new patient types, the female patient and the elderly patient, in whom physicians anticipate increases in the use of Prozac. These new patient types also allowed the message to elaborate on key Prozac features and benefits as well as to provide context and credibility to the safety record of Prozac (e.g. largest antidepressant safety database in pregnancy).

To further avoid merely confirming physicians' experiences with Prozac, the team bolstered the power story with data from two new comparative trials.

- One study showed that patients on Prozac maintain complete remission for a longer period of time than those on its SSRI competitors.

- Another study showed that Prozac was effective in a majority of patients who did not respond to Zoloft. PSYCHs found the Zoloft data particularly interesting; however, this information did not move the PCPs, who see fewer treatment-resistant patients.

In order to engage primary care physicians and psychiatrists and to meet the objection that the Prozac message does not speak to them, the developed messages added set-up language. For primary care physicians, this language was "today, primary care physicians are being more aggressive in diagnosing and treating depressed patients." In contrast, for psychiatrists, the set-up idea was "your depressed patients are complex and challenging."

In order to broaden the number of depressed patients that PCPs perceive as requiring a boost of energy, the developed message inserted the idea that "fatigue and lack of motivation are two of the most common complaints of depressed patients, affecting two-thirds or more."

Because some physicians doubt that "Prozac is the best choice for re-energizing depressed patients"—in part because of the need to individualize therapy and also because there are atypical antidepressants such as Wellbutrin that are also activating—the developed messages present Prozac as a "tool that can be powerful and versatile" in the hands of the physician. This acknowledges the role of the physician at the outset of the selling story.

Reflecting the reality that many physicians present treatment options to their depressed patients, the developed message closes with a question: "Would you consider discussing Prozac as a treatment option for depressed patients?" The team dropped the sometimes controversial claim of the starting message that "92% of patients taking Prozac report being satisfied."

Reinforcing the importance of the patient who requires a boost of energy, PCPs are intrigued by a statement citing the magnitude of this group: two-thirds or more of all depressed patients. This statement works well in setting PCPs up for the efficacy information that follows.

Reminding physicians of both specialties of the full array of dosage forms for Prozac proves very valuable in conveying the notion that Prozac is versatile and can be used in a variety of situations. This also reminds a significant number of physicians of the 40 mg capsule that was made available last year. The mention of the 10 mg scored tablet enhances the previously-mentioned idea that Prozac is appropriate for use in the elderly.

FLOW OF THE DEVELOPED PCP AND PSYCH MESSAGES

The developed messages position Prozac as a powerful and versatile tool, offering clinical data to prove its superior efficacy and safety, especially in three patients types which differ somewhat between the PCP and PSYCH messages. The PCP message leads the tired and unmotivated patient, while the PSYCH message leads with the complex, partial and non-responder patients. Subsequently, both messages set out to prove Prozac's superiority in female patients with special risks, and elderly patients with co-morbidities and polypharmacy.

The basic flow of the messages is as follows:

Message Section	PCP Message	PSYCH Message
Set-Up	Acknowledgement of PCPs' growing role in the diagnosis and treatment of depression; assertion that Prozac is a powerful and versatile tool	
	Identifies the complex patient subgroups discussed in the message and asserts that Prozac is a powerful and versatile tool	
Efficacy and Safety	Prozac is particularly effective and easy to use in patients requiring a boost of energy	
	Prozac is able to address the needs of non-responders	
	Female patients may have special risks that Prozac can address safely and efficaciously	Same
	Prozac is safe and effective for geriatric patients and others on multiple medications	Same
Ease-of-Use		

Prozac has several dosage forms for your convenience

Same

OVERALL REACTIONS TO THE PCP MESSAGE

Overall, PCPs say that the message clearly reminds them that Prozac is a powerful antidepressant with efficacy in a variety of patient types.

Across the three market segments (Faders, Undecideds and Enthusiasts) physicians appear to read the PCP message similarly. Generally, all three market segments report that the message is valuable because it informs them of new FDA indications and it reminds them that Prozac is the gold standard for antidepressant therapy: tried and true. The message communicates that Prozac is safe in a broad spectrum of patients and that although one dose is effective in many patients, the agent does have dosing flexibility. It also informs PCPs that Prozac is more effective than other SSRIs in some patients, such as those with low energy, and that it is safe in female patients and the elderly.

> *Prozac is the only one with the indications and it is safe across a broad spectrum of patients. One dose works in a lot of people and dosing is flexible. These are all reasons to go back to using it. There are more patients I could be using it in. (PCP – Fader)*

> *It is the gold standard in treating depressed patients. Prozac is more effective in certain groups than other SSRIs. It is also safe to use in pregnant women and geriatric patients, which I had thought the opposite was true. (PCP – Undecided)*

> *This is a powerful case. It shows flexibility with doses and it's tried and true. Prozac probably has the most powerful bang for your buck. (PCP – Enthusiast)*

After reading the message, Faders and Undecideds, in particular, are inclined to use more Prozac, particularly for women and the elderly.

After reviewing the message, PCPs most frequently assert that the information regarding safety in the elderly would make them more inclined to use Prozac rather than Zoloft in this population. They explain that Prozac's energizing effect would often benefit this population; however, concerns about Prozac's safety has made them reluctant to use it in the elderly. In addition, some PCPs say that the message reminds them of Prozac's long half-life, and this information causes them to project use of Prozac over Paxil. The message causes a few PCPs to conclude that when patients fail another SSRI, they would try Prozac before trying Effexor, because Prozac is powerful and easier to use.

> *Zoloft has been my drug of choice in the elderly population. However, according to this, Prozac is just as safe. Patients can miss doses and it is also safer in pregnancy. (PCP-Fader)*

> *If I can go to the 40mg dose of Prozac for improved efficacy, as long as it is not too expensive, I would keep more patients on Prozac longer before going to Effexor. (PCP-Undecided)*

> *Prozac's long half-life is a major advantage over Paxil, and a good reason for choosing Prozac as a first-line agent before Paxil. (PCP-Fader)*

Most PCPs state that low-energy patients comprise the largest group of their depressed patients, but, since they are already using Prozac in these patients, the message does not cause them to project significant additional use for them. In addition, PCPs reject the characterization of female patients as the only ones who present with this symptomatology.

> *Yes, it is true that Prozac is the most alerting of the SSRIs, and where it is an excellent drug is in my patients who are more retarded-lethargic. (PCP-Enthusiast)*

> *Female patients have risks and comorbidities, true, but their presentation is not different from men. (PCP – Enthusiast)*

The following chart summarizes the PCP allocations and reallocations of antidepressant usage before and after reading the developed Prozac message. Reduction in use of Effexor and Paxil seems to reflect the energizing power of Prozac and Zoloft.

Therapy	**Before Prozac Message**	**After Prozac Message**	**% Change**
Prozac	21	25	+4
Celexa	14	14	0
Effexor	13	12	-1
Luvox	1	1	0
Paxil	17	16	-1
Remeron	3	3	0
Serzone	7	7	0
Tricyclics	1	1	0

Trazodone	
	3
	3
	0
Wellbutrin	
	11
	11
	0
Zoloft	
	14
	12
	-2

A few PCPs mention that some of their patients are reluctant to accept Prozac due to Prozac's perceived side effects, such as loss of libido, violent behavior, and suicidal tendencies. In addition, PCPs mention that other medications, such as Effexor and Paxil, have developed strong niches in the market, which favorably influences their use of those medications in certain populations.

> *You have made a strong case here. Prozac probably gives the biggest bang for the buck of all the SSRIs. The reason I don't write it more is that there are good niches for other drugs, for example, Effexor in GAD and Paxil in Anxiety. (PCP-Enthusiast)*

SECTION-BY-SECTION REVIEW OF THE PCP MESSAGE

The opening statement in the PCP message engages physicians because it recognizes their increasing role in the treatment of depression.

- Today, primary care physicians are being more aggressive in diagnosing and treating depressed patients.

PCP's agree with the first statement in the message and feel that it is a fact. They note that because the drugs are now easier to use, the awareness and treatment of the disease is higher. This heightened consciousness of the disease, they indicate, has resulted in more aggressive depression screening in the primary care setting. They are glad to hear that their more aggressive role is accepted.

> *I just feel that that's a statement of fact. That's true. No argument there. That's what I think I mentioned earlier myself. I think that I'm doing that, and I would expect most other doctors are, too. They're more aggressive, because they've got drugs that are relatively easy to use, so consciousness of the diagnosis and treating it is greater. (PCP – Enthusiast)*
>
> *We are looking for it now, as we should. (PCP – Enthusiast)*
>
> *I am glad to hear that our new role is accepted. (PCP – Fader)*

The core positioning idea, "power and versatility," often confirms PCPs' perceptions of Prozac, especially for tired, unmotivated patients.

- In your hands, Prozac can be a powerful and versatile tool, particularly for depressed patients who are tired and unmotivated, female patients, and the elderly.

The typical PCP reaction is to say that Prozac can be powerful for many patients, not just the elderly and women. PCPs often note that many depressed patients present with fatigue and lack of motivation. Therefore, they sometimes wonder why female or elderly patients are being singled out. They commonly mention that male patients can present with these same symptoms.

> *Prozac is powerful for all patients: males, younger ones, even. These are not the only patients that present with these symptoms. (PCP – Undecided)*

> *When I first saw that, why are they talking about female patients? I had never singled female patients out for Prozac and I didn't know what they were talking about. Many patients are tired and apathetic. (PCP – Enthusiast)*

However, the alternative positioning, "short-term power, long-term protection" causes dissonance.

v In your hands Prozac provides short term power, long term protection for three distinct depressed patient types:

PCPs claim that the meaning of the phrase, "short-term power, long-term protection" in the alternative message is confusing and leads to questions about Prozac's power. In particular, others comment that the "short-term power" portion is a "little heavy" or sounds like "sales" language.

> *When we talk about a drug, we usually say that something is more effective or efficacious. When you start talking "short-term power, long-term protection," that sounds more like a catchy sales phrase than it does a description of a medication. (PCP – Undecided)*

PCPs agree with the prevalence of fatigue and lack of motivation in depression, and feel this statement sets the stage for what is coming next.

v Fatigue and lack of motivation are two of the most common complaints of depressed patients, affecting an estimated two-thirds or more. In addition, some have vague aches and pains. These symptoms can impair functioning at work and at home.

Overall, the majority of PCPs simply say that the statement feels like a context setter for what is to come. They overwhelmingly agree that fatigue and lack of motivation are indeed the most common complaints of depressed patients. In fact, some note that it is the somatic symptoms themselves that often lead to a diagnosis of depression. A few also note that irritability and insomnia can also be a symptom of depression. A few would prefer the word apathy to the phrase "lack of motivation".

> *That's basically what happens. It didn't strike me as typically positive or negative, one way or the other. It's just a statement of fact. (PCP – Enthusiast)*

> *I agree. That's true. I think that's my experience. [And about the vague aches and pains]…That's for sure. A lot of patients come to the office not complaining of depression, of course, but complaining about a list that goes on and on of somatic complaints, and pain, discomfort, and all this sort of stuff is a large part of it. Often the diagnosis of depression is arrived at because of the list of complaints rather than the patient coming in and complaining of their mood. (PCP – Enthusiast)*

> *Irritability and insomnia are symptoms of depression as well – important symptoms. (PCP – Fader)*

> *Yes, there is general malaise, but I think apathy is better than lack of motivation. (PCP – Undecided)*

Most PCPs report seeing a clinical impact after two to four weeks of treatment and are sometimes skeptical that improvements can occur in only one week.

> At 20mg QD, Prozac is so effective that patients may start to see improved energy and concentration as early as one to two weeks, as shown in large-scale, placebo controlled studies.

The majority of PCPs agree that Prozac works quickly; however, many of them say that improvement in one week is a bit optimistic. Only a small minority are actually offended at the suggestion of efficacy in just one week.

> *I'd say that's probably true…it takes two weeks, usually, though. Two to four weeks is more realistic. (PCP – Fader)*

> *Two weeks is a bit on the short side…but it's true; I've seen patients at about two weeks…I usually give them samples for two weeks after they come back, and try to encourage them to continue on at that point in time and indeed some patients do notice a significant improvement already in two weeks. (PCP – Enthusiast)*

> *One week? That is different from what the journals say and from my own clinical experience. I disagree with this statement. (PCP-Undecided)*

The "Prozac does not require titration" statement that was in the alternative PCP message is rejected by PCPs, as it is not in concordance with clinical experience.

> Prozac does not require titration, unlike Celexa and Zoloft according to databases reflecting actual clinical practice, making it more convenient for you and your patients to get the short term results

In addition, some PCPs take exception to the claim that "Prozac does not require titration," as used in the alternative version, insisting that in their clinical experience, Prozac does require titration, although perhaps not as much as other products.

> *I don't agree with the fact that Prozac does not need to be titrated at all. I have lots of people that take all different sorts of doses after titration after a while. Maybe titration is not as big a factor as it is with some of the others. I would agree you usually don't have to go to a super-high dose. (PCP – Undecided)*

> *I disagree with that, because I do think it does require titration: many of my patients do require more. For patients that I start with 20 mg for general depression, a fair percentage of them need to go on the higher dosage. And I do see benefits at a higher dose, so I think there is some titration. (PCP – Fader)*

I usually start them on 20 mg and the majority of patients stay on 20 mg. An effective dosage so we don't have to bring patients back more frequently and try to figure out what dosage will work for the patient. (PCP – Fader)

PCPs find the dual metabolite information confusing, so the team removed it from the message during the refinement phase.

> The potency of Prozac is linked to the unique dual efficacy of fluoxetine and its equally potent metabolite, nor-fluoxetine, reducing the likelihood of upward titration.

PCPs are confused when they read the information on Prozac's dual metabolite. Although the majority of them accept the information at face value, they do not know its clinical significance. A few even wonder if the dual metabolite would worsen Prozac's side-effect profile. Therefore, removal of this information from the message has no detrimental impact on Prozac's power and versatility message.

I'll just take it for what it says. It's just a general statement on the active ingredients, and I wouldn't dispute it, but it doesn't necessarily say or mean a whole lot to me. (PCP – Undecided)

Often the breakdown product can be a double-edged sword. On one hand, the point can be made that that makes it more effective. On the other hand, a point can be made that that can potentially double the side effects. (PCP – Enthusiast)

PCPs agree that Prozac needs titrating less often than other SSRIs, so this statement differentiates the product and augments the power story for most.

> Therefore for the majority of your patients, the Prozac 20mg starting dose gets patients well and keeps them well, which is less often true for Celexa and Zoloft according to databases reflecting actual clinical practice.

Overall, PCPs agree that Celexa and Zoloft require titration more often than Prozac. This is an added advantage for a few physicians who comment that needing to titrate the patient's medication can make the patient lose confidence in the treatment and become skeptical of its ability to help.

> *I believe that. I believe that Celexa and Zoloft do need titration more often than Prozac. So I accept that. (PCP – Enthusiast)*

> *I think I mentioned that to you before…when you have to titrate doses, patients tend to lose confidence in the drug and they think it's not working, even if it does ultimately work for them…they are suspicious…the confidence of the drug is diminished. (PCP – Enthusiast)*

However, a few PCPs question how important it is that the starting dose of Prozac is the dose on which most patients stay. They feel that the starting dose is not as important as the head-to-head efficacy of the competing antidepressant therapies.

> *I question whether going head-to-head with Celexa and Zoloft about the starting dose is what we need to be looking at. The real question is whether or not they stayed on Prozac or Celexa or Zoloft for a longer period of time. Not necessarily [the efficacy of] the starting dose. (PCP – Fader)*

In addition, some note that they have not needed to titrate Celexa, either. A few physicians remark that Paxil is missing from this comparison and deduce that the reason for this is that Paxil, similarly to Prozac, does not often need to be titrated.

> *I have not had to go up with Celexa. (PCP – Enthusiast)*

> *That means Paxil probably does the same thing as Prozac or would have titrated too. (PCP – Fader)*

The "stay on Prozac longer" statement enhances PCPs' perception of the Prozac's efficacy and tolerability.

In fact, prescription claims studies have also shown that patients stay on Prozac longer than on Zoloft, Paxil, and Celexa, providing a greater chance of sustaining remission over the long run.

PCPs agree that the full length of therapy is ideal for patients, and ultimately more effective. Hence, the majority of PCPs are very interested in this statement, and many speculate about why this could possibly be so. A significant number of PCPs hypothesize that it could be due to Prozac's tolerability.

> *This is a highlight of the page. I did not know. Of course it is always better if the patients stay on for the full length of therapy. (PCP – Fader)*

> *Why do they stay on the therapy longer? I need to see this data. (PCP – Undecided)*

> *This makes me think that Prozac is a well-tolerated compound. (PCP – Fader)*

Interestingly, physicians who have seen the data before appear to be even more comfortable with this assertion, acknowledging the logic of the supporting story about lack of patient confidence.

> *My reps have shown me those data and that I can accept also. That is sales data that I've seen. They claim that. I think I mentioned that to you before....when you have to titrate doses and whatnot, patients tend to lose the confidence in the drug and they think it's not working, and that kind of destroys the....even if it does ultimately work for them.....they are suspicious.....the confidence in the drug is diminished. (PCP – Enthusiast)*

PCPs view Prozac's long half-life and lack of discontinuation syndrome as a key differentiating attribute from Paxil and Zoloft.

> Prozac also protects patients from the re-emergence of depressive symptoms and discontinuation side effects due to missing doses or stopping the medication.

PCPs agree that Prozac, because of its long half-life, does not have the discontinuation effects found with other antidepressants. Some physicians specifically state that the fact that patients can miss a

dose without experiencing discontinuation side effects is a reason to write for Prozac. When reading this statement, they often mention that Paxil does have these side effects.

I know Prozac has capitalized on the long half-life to make that claim, whereas Paxil has been accused of discontinuation syndrome with its short half-life and possibly having significant symptoms if patients miss a day or two of the drug. So, this is accepted generally, too…this is not a problem. (PCP – Enthusiast)

Half-life is one of the biggest benefits. Discontinuation syndrome – missed dose is one of the biggest reasons to write for Prozac. (PCP – Enthusiast)

I think it's one of the big positives of Prozac – the side effect on missing doses, especially. It really makes a big difference. I think that I would be more upfront about the lack of withdrawal, because I think it is a big issue with Paxil, and Zoloft, to a slightly lesser degree. I think it's a big deal and I don't see it mentioned here.. (PCP – Undecided)

PCPs question the exclusivity of females presenting with fatigue and lack of motivation.

- Female depressed patients often present with fatigue and lack of motivation, and some may also have special risks and comorbidities.

PCPs feel that many patients, not just females, present with fatigue and lack of motivation. While they agree that pregnancy is a special risk, they are unsure what comorbidities are being referenced.

Well, I think they're just like everybody else. Females. Male - female, the same symptoms: lack of motivation and fatigue, that's reasonable. Special risks and comorbidities: I presume … pregnancy...that's true. (PCP – Enthusiast)

Well, everybody presents with fatigue and lack of motivation, so I didn't know that 'female' naturally meant that, but they may have some special risks, especially with pregnancy. (PCP – Fader)

The pregnancy database information enhances the perception of Prozac's overall safety.

Prozac has the largest antidepressant safety database in pregnancy, which provides reassurance for those female patients who may have unplanned pregnancies

A significant number of PCPs say that the pregnancy database information might cause them to make Prozac their first choice among women of child-bearing years. Also, some PCPs say that they will use this information to explain to Prozac-resistant patients just how safe the drug is. More than a few PCPs wonder whether or not patients can stay on Prozac throughout the pregnancy. A few question in which category the medication is placed.

I can tell my female patients about the database. I can tell them that many other women have had no problems. (PCP – Enthusiast)

Use in pregnant women is reassuring. It makes me wonder why it can't get an upgraded pregnancy rating. (PCP – Enthusiast)

The general pregnancy database stating that Prozac has the largest antidepressant safety database is more compelling to PCPs than the more clinically-focused version, which includes the size of the database. When the more complex version is used, PCPs begin to lose focus on the overall purpose, shifting their attention to specifics about outcomes.

It doesn't really say that it's safe to use in pregnancy. It just says that there is a lot of information on women using it on pregnancy. Is it safe if I become pregnant? (PCP – Fader)

It's helpful to know. People can potentially become pregnant while they're on any drug, and if they're going to be on it for a long period of time, if that should happen, you'd like to know that the chances of some kind of teratogenic effect is minimal. Of course, it doesn't say if the outcomes are good or bad, it just says it has 2,000 in the database. It could have 1,000 bad outcomes: you don't know. You assume it's good or they wouldn't mention it. (PCP – Undecided)

The weight gain/unwanted sedation statement serves as a positive reminder of Prozac's benefits for female patients.

While individual patients vary, Prozac is generally well tolerated and is usually not associated with unwanted sedation or weight gain.

PCPs state that their female patients are concerned about these side effects, particularly the weight gain, and will sometimes discontinue other medications because they cause weight gain. Overall, PCPs agree that for most patients, Prozac does not cause weight gain or sedation. However, a few note that they occasionally have patients who do suffer these side effects. For a few others, this statement brings to mind the side effects Prozac does have: particularly, overstimulation, increased anxiety and insomnia.

I agree that Prozac does not cause unwanted weight gain. Weight gain is a big deal in females and reason for discontinuation. (PCP – Enthusiast)

The fact that Prozac does not cause unwanted sedation or weight gain is reasonably true. I'd say about 65% of patients on Prozac don't get sedation or weight gain. I think this is a plus on their part. (PCP – Enthusiast)

It is true, generally, of the lack of weight gain and sedation side effects. But, I do worry about overstimulation, increased anxiety, insomnia. (PCP – Fader)

The indications for PMDD and bulimia often sparks PCPs' interest.

Prozac has been shown to treat both the mood (irritability and dysphoria) and physical symptoms (breast tenderness, bloating) of Premenstrual Dysphoric Disorder and is the only drug approved for this indication by the FDA.

Prozac has been proven to reduce both binge eating and vomiting associated with bulimia and is the only agent approved by the FDA for this indication.

PCPs find the information relating to efficacy in PMDD particularly interesting. They are especially curious about how it helps the physical symptoms and how the medication is dosed.

> *I would like to know if they have to stay on a whole month or not. I would assume that they didn't, since it has such a long half-life. Do they have to take it chronically or just 2 weeks out of the month? (PCP – Fader)*

> *The physical symptoms are new to me. Is it a direct effect on physical symptoms or lowering the threshold? (PCP – Fader)*

While PCPs claim to see few bulimic patients, they say that the FDA approval would cause them to make Prozac their drug of choice for this patient population.

> *I am not aware of a specific FDA indication if someone has a solid eating disorder. I do tend to prescribe Prozac. (PCP – Fader)*

> *I can accept that, although I don't see much eating disorders in my practice, and I don't have any personal experience with the drug for that indication…but I believe that's true; it has an indication for that, but it is not an area of great interest for me, because I don't see it too much. (PCP – Enthusiast)*

PCPs report that approval for Prozac in these indications makes it easier for them to justify usage to patients and affords additional medical/legal support for their decision to prescribe it.

> *See, the FDA indications may not change my practice but it is something I can tell my patients that may make Prozac more acceptable. (PCP – Fader)*

> *We've used it, but I did not know it had an official FDA approval. To me it means a lot: you are always nervous if someone has an unfounded effect, and you are giving them an unapproved drug for an indication, then you are pretty much liable for everything that happens. You can still be liable, but if at least it is an approved indication, I think you have a better foot to stand on. (PCP – Undecided)*

The safety-in-the-elderly section generates new interest in Prozac among many PCPs.

Prozac is proven safe and effective in geriatric depression, the only antidepressant with formal FDA approval for these patients

As all patients get older, their renal function declines. Unlike other antidepressants, Prozac does not accumulate and lead to increased side effects in the elderly.

The section on safety in the elderly results in the anticipation of the greatest numbers of prescriptions for Prozac. In general, PCPs seem more willing to accept the safety-in-renally-insufficient information. However, a few PCPs do question how a drug can have a long half-life and not accumulate.

The information about accumulation means it is safe and this makes me think it may work a little bit better in the elderly than the Zoloft I was using. (PCP – Fader)

I knew a patient's renal function declines…I did not realize that Prozac did not accumulate in those patients. Then that may be one reason to use it more in the elderly. (PCP – Fader)

I don't know how that works. I read that – because the page before, you told me it had an active metabolite, you have a steady state. And it would appear to me, if that were the case, then how does it not accumulate in renal failure? …then I figured it had to be cleared by the liver. That's the only way that their statement can be true. So, other antidepressants must be cleared by the kidneys for them to accumulate. So that's what my mind thought as I read that. Gotta be hepatic clearance on that. You don't say that, but that would be the only way that that could be true. (PCP – Fader)

Well, that is also a little bit of a concern since Prozac has such a long half-life. You would think that the drugs with a shorter half-life would be less likely to have the problem than Prozac…so again, that means a little more explanation for me. (PCP – Enthusiast)

PCPs do not question Prozac's safety for elderly patients taking multiple medications or being treated for other concomitant conditions. In fact, most PCPs expect Prozac to be safe and effective in these patients. The fact that Prozac is the most studied is linked back to the fact that Prozac has been on the market the longest.

All I see is diabetes, post-MI and cancer, so that's important for me to know. (PCP – Fader)

I can accept that …it's been around the longest…I would expect it is. Those are a lot of the patients I'm treating. (PCP – Enthusiast)

I like the multiple medication point – that was the one that caught my eye more than the other, because I'm using it for depression, and obviously I expect it to work for depression…but the fact that it's shown to be safe with multiple medications – that was one of the points I brought to you on why I like to use lower doses of the Paxil…because lower dose is less likely to be in medication problems…and you're telling me that you've already done studies which show it is safe on multiple medications. So that's important for me to know. Because that was one of the reasons I was using a competitor. (PCP – Fader)

PCPs acknowledge the difficulty of treating severely ill patients; however, it comes as no surprise that Prozac is effective in these patients.

Prozac is the most studied antidepressant in depressed patients with concurrent medical conditions such as diabetes, post-MI, cancer, and HIV.

- Prozac was effective at relieving depression in these patients
- Prozac was shown to be safe and well tolerated in these often debilitated patients on multiple medications.

PCPs acknowledge that because these patients are suffering from concomitant conditions and on concomitant medications, they are often more difficult to treat. The majority of PCPs expect Prozac to be safe and effective in such patients, mainly because it has been on the market the longest. Therefore, it has had the greatest opportunity to be studied with this population.

Prozac's been around the longest; it has had the greatest chance to be studied. (PCP- Enthusiast)
This seems logical, given how long it's been around. (PCP - Undecided)

I can accept that. It's been around the longest. I would expect it is. (PCP – Enthusiast)

However, a few physicians express some surprise that Prozac is safe in these patients, thinking that other SSRIs would be safer than Prozac for patients on concomitant medications. A few others claim that all of the SSRIs are equally as safe in this group.

The fact that it's shown to be safe with multiple medications – that was one of the points I brought up to you on why I like to use lower doses of Paxil...because lower dose is less likely to be a medication problem. You're telling me that you've already done studies which show it is safe on multiple medications. So that's important for me to know. (PCP -- Fader)

Folks like me tend to avoid Prozac in these patients. (PCP – Fader)

I thought Zoloft would be safer. (PCP -- Enthusiast)

Almost any of the SSRIs are safe. I don't worry about drug interactions. (PCP – Fader)

The multiple dosage form information adds to PCPs' perception that Prozac is easy to use.

Prozac has the flexibility to start at 10 mg in the elderly Prozac is available in several dosage forms, including 10 mg scored tablets, 20mg and 40 mg capsules, and even a liquid formulation

PCPs state that the flexible dosing of Prozac may reduce their likelihood of switching patients to another antidepressant. The ability to start as low as 10 mg makes Prozac an attractive choice for the elderly. A few PCPs say that knowing that a 40 mg dose of Prozac is available may cause them to increase the dose of the drug before switching inadequately-responding patients to Effexor. Some PCPs say that they find the liquid formulation to be especially useful in nursing-home patients.

This is reminding me and making me more willing to try it in the elderly. Prozac gives more dosages, too; I did not know about the 40 mg. (PCP – Fader)

I've got a fairly big nursing-home practice, and that would be a useful thing. Some people that have had bad strokes and they can't speak, and they're on tube-feeding, they still can be depressed, and that can be a useful thing, to be able to give it in liquid form. (PCP – Undecided)

PCPs indicate that the message provides them with some new and valuable information about Prozac.

v Given Prozac's power and versatility, would you consider discussing Prozac as a treatment option for depressed patients who are tired and unmotivated, or female, or the elderly?

The majority of PCPs respond affirmatively to this question. PCPs most often cite the information about Prozac's use in elderly patients as new information. Particularly for some Prozac Faders this information has the potential to motivate them to consider Prozac more often for their elderly patients. For the majority of Prozac Undecideds and Enthusiasts, this message reinforces their current use of Prozac.

> *It has not been my practice to prescribe this for the elderly, but the statement about renal function, I'd think about it. (PCP – Fader)*

OVERALL REACTIONS TO THE PSYCHIATRIST MESSAGE

The majority of PSYCHs say that the message reminds them of why they consider Prozac to be an excellent SSRI, and many are intrigued with new information presented.

After reading the message, most PSYCHs agree that the adjectives "powerful and versatile" are truly characteristic of Prozac. The majority of PSYCHs already consider Prozac to be a "powerful" antidepressant, more powerful than Zoloft and Celexa in particular. They feel that the agent is the

gold standard in antidepressant therapy and this information supports that impression. In addition, PSYCHs say that the word "versatile" refers to the broad range of patients for whom Prozac is appropriate, as well as the range of dosage forms in which Prozac is available. Specifically, they agree that Prozac is a good agent for use in women, elderly with comorbidities, and in some non-responders.

> *Sometimes I forget that it works well. It has been around and it works – especially in certain types of patients like bulimics. Prozac is the gold standard. There is nothing I can argue with here. (PSYCH)*

> *It is effective across a broad spectrum of patients in clinical situations, and it has the significant data to support that. And by situations, I'm including both patient population and diagnosis. (PSYCH)*

> *This reminds me that Prozac is good in a wider range of geriatric and more complicated patients. (PSYCH)*

> *The flexibility of dosing is very, very important, because it allows you to mess around with the dosing. A lot of times it gives the patients a feeling that they have some control over it. I can go down 5 mg or up 5mg or something like that, and the patient feels they have some control over it. And that is good for helping them stay on the medication. (PSYCH)*

The message consistently succeeds in compelling PSYCHs who are low-Prozac prescribers to increase their usage in female and elderly patients, especially at the expense of Zoloft.

Those PSYCHs who project an increase (typically high-users of Zoloft) explain that their usage in elderly patients and women will grow, primarily at the expense of Zoloft and Celexa. In addition, a few say they would substitute Prozac for Effexor in some instances, because of Prozac's high success rate, its possible effect on norepinephrine, its 40-mg dosage strength, and better tolerability profile. A few PSYCHs say their use of Wellbutrin may be slightly reduced, as inclination to utilize expensive combination therapy may diminish based on the power story contained in the message.

Interesting, I always thought of Prozac as an SSRI. I didn't know it could challenge Effexor. (PSYCH)

I was not aware that Prozac had an effect on norepinephrine. It would be interesting if it follows the same response patterns that we get with Effexor. (PSYCH)

This would make me think of Prozac more in my geriatric population. I have been using Zoloft almost exclusively in these patients because it circumvents the CP 450 system. (PSYCH)

I would reduce my Zoloft prescribing because it is closest to Prozac in my mind. The information on side effects in the elderly and the specific indication for this group would give me more confidence. (PSYCH)

The following chart summarizes the mean estimates of the percentages of depressed patients on different types of therapies before exposure to the developed Prozac positioning story and then the changed estimates after exposure to the Prozac information. Physicians assume the Prozac information is accurate and supportable by clinical research and publications. The pre-Prozac PSYCH columns add to more than 100% because some PSYCHs have patients on combination therapies. The after-Prozac columns reflect only the change from the current therapy, and, due to rounding, do not total to 0.[2]

Therapy	**Before Prozac Message**	**After Prozac Message**	**% Change**
Prozac			
	20		
	24		
	+4		
Celexa			
	16		
	15		

[2] These mean percentages are merely directional information for qualitative insights and are not projections of the market share.

	-1
Effexor	
	9
	8
	-1
Luvox	
	3
	3
	0
Paxil	
	12
	12
	0
Remeron	
	4
	4
	0
Serzone	
	7
	7
	0
Tricyclics	
	2
	2
	0
trazodone	
	12
	12
	0
Wellbutrin	
	17
	16
	-1
Zoloft	
	15
	13
	-2

However, most of those who do not anticipate a change consider themselves to be high users of Prozac and comment that the message offers little information to expand their usage into new areas. PSYCHs explain that Prozac would be inappropriate for patients who are anxious-depressed or who require sedation. In addition, some PSYCHs say that increasing the dose of Prozac would be prohibitive for some of their patients, due to increased cost. A few PSYCHs mention the presence

of comorbidities such as smoking or ADHD, which may lead them to favor the use of other antidepressants.

SECTION-BY-SECTION REVIEW OF THE PSYCH MESSAGE

The PSYCH message introduction does not effectively engender interest to read on.

- Your depressed patients are often complex and challenging
  - Partial and non-responders
  - Female patients with special risks
  - Elderly with medical comorbidities and polypharmacy

Psychiatrists acknowledge that their partially- and non-responding patients; female patients with special risks; and elderly with medical co-morbidities and polypharmacy are complex and challenging. However, many simply ignore this information, regarding it as an obvious attempt by Lilly to understand and connect them. In addition, they are not sure what "special risks" women may have at this point in the message.

It's true; these are challenging patients, but it seems just a way to try to connect with me. (PSYCH)

What special risks are they talking about? (PSYCH)

This feels like a slippery attempt to show they understand me. (PSYCH)

Psychiatrists agree that Prozac is powerful and versatile but when they read the statement, tend to say that it is just marketing language.

- In your hands, Prozac can be a powerful and versatile tool for such patients.

Psychiatrists appear to agree that this statement is true *prima facie*; however, they resist the point because they often perceive it to be "marketing". To them, versatility refers to the variety of doses and the ease of combining Prozac with other therapies, but this is not new information. They do agree that Prozac is powerful, often referring to it as the gold standard in depression; however, in this context, the assertion of power has not yet been established, and is not distinguishing.

Okay, but what are they getting at? This is marketing. (PSYCH)

Prozac comes in a wide range of doses, can be combined with other medications: this is sort-of true, but so what? That's nothing new. (PSYCH)

Well, that is true. Prozac and other antidepressants on the market are powerful. (PSYCH)

Prozac is the gold standard. (PSYCH)

New information about Prozac's effect on norepinephrine/dopamine is of major interest to PSYCHs and leads them to seek more information about the clinical impact and dosages.

- Patients who are partial or non-responders are particularly challenging to treat
  New scientific data prove that Prozac has added activity on the norepinephrine and dopamine systems at higher doses

The majority of PSYCHs feel that the activity on additional receptors could make Prozac appropriate for more patients and thus allow it to challenge the market share of Effexor, which is viewed by physicians as being more efficacious than the SSRIs. Many indicate that this is new information to them and that they would like to see details about dosing as well as data regarding the clinical impact. When the message was tested without this information, it seemed to lead to more skepticism toward Prozac's power, on the part of PSYCHs.

I think some people need a noradrenergic or dopaminergic component where the reuptake is more available. So it might be good if Prozac had that intrinsic characteristic. (PSYCH)

I did not know this [norepinephrine and dopamine effect]. It means Prozac can challenge Effexor. It is not just an SSRI – you get three bangs for your buck, so to speak. (PSYCH)

I want more information: what are the doses? It would be interesting to see if we see the same response as with Effexor. (PSYCH)

Many PSYCHs believe the statement regarding the increased likelihood of remission with 40 mgs; many also explain that inadequate dosing accounts for many treatment failures.

> Prozac, in recently completed clinical research, significantly increased the likelihood of complete remission (57%, $p<.05$) and also sustained remission over the long term (for at least the 6 month duration of the study) in struggling patients whose dose went from 20mg to 40mg QD

PSYCHs note that increasing the dose of Prozac will generally bring about a greater response. They complain that clinicians should know that some of the patients need more medication than others do. A few note that other antidepressants make similar claims regarding response at higher doses.

I thought that the problem with this is that the clinicians doing this didn't realize the patient needed more medicine. It doesn't surprise me that the patients needed 40, 60, 80 mg of Prozac to achieve remission. (PSYCH)

Sometimes going from 20 to 40 mg of Prozac really makes a difference. (PSYCH)

Paxil and Effexor make the same claims: that you get more response at higher doses. (PSYCH)

Psychiatrists find the lack of discontinuation side effects to be an advantage specific to Prozac.

> Prozac also protects patients from the re-emergence of depressive symptoms and discontinuation side effects due to missing doses or stopping the medication.

The most attractive information in this statement concerns Prozac's lack of discontinuation side effects, which psychiatrists generally find to be an advantage in comparison to agents such as Paxil and Effexor, and perhaps Celexa. For patients who are non-compliant, Prozac's long half-life is a benefit. However, a few indicate that they do not see a problem with discontinuation-side-effects in competing agents.

Yes, that is one of the advantages that Prozac has. (PSYCH)

This is true in the short term, especially versus Paxil and Effexor. (PSYCH)

The long half-life is a major advantage in patients who are non-compliant or who've had withdrawal effects before. (PSYCH)

If they miss a dose or two, it's not a real problem if the patient is generally reliable. If they take a couple of doses here and there, they run into the problems of efficacy, not necessarily discontinuation side effects. It's true of Paxil and Effexor in my experience too. (PSYCH)

Many PSYCHs attribute the "stay on Prozac longer" information to its long half-life.

> In fact, prescription claims studies have also shown that patients stay on Prozac longer than on Zoloft, Paxil, and Celexa, providing a greater chance of sustaining remission over the long run.

The "longer duration" information intrigues physicians and generally generates some positive responses. Some physicians even conclude that Prozac's long half-life will permit patients to miss doses without compromising efficacy or causing withdrawal syndrome. For a few PSYCHs, this information implies that patients stay on Prozac longer, in spite of the side effects, because it is effective in relieving their depression. Only the fact that this information was garnered from a prescription claims study arouses questions.

I think the long half-life really is an advantage. A lot of people get withdrawal if they are on high doses of Zoloft and then stop it suddenly, and they have more side effects from it. Celexa is fairly new; I don't know about that. But I know its half-life is more like Zoloft's: it's shorter. (PSYCH)

I'm fascinated with this idea that patients stay on Prozac longer than those other ones. I can't account for why that is. For example, I think a higher percentage of patients complain of sexual dysfunction with Prozac than any of the others. Yet, even then they tell me "Doc, I feel so much better with this stuff." I don't have that as much with the competition. There really is a certain degree of loyalty. The patients just don't want to go back there. That Prozac may be doing more than treating depression. It may actually be doing more than other SSRIs as far as affecting some underlying alpha male or alpha female sort of issues. (PSYCH)

I think I need more data about what that means. I'm suspect of prescription claim studies. I would just like to see how they did that study. I'm not saying it's not true. It would be interesting if they showed the actual data. But it is a study, which is subject to interpretation: how the study was done, the total number of prescriptions that the pharmacy shows for months and months (PSYCH)

While the Zoloft non-responder information is intriguing, PSYCHs express a high degree of skepticism.

> Prozac, in another recent clinical trial, was effective in reducing the total HAM-D score by at least 50% in a majority (63%) of 106 Zoloft non-responders.

For the majority of PSYCHIs, this statement inspires skepticism. PSYCHIs wonder what doses were used in the comparison and what happens when Prozac non-responders are placed on Zoloft. However, many PSYCHs admit that Zoloft non-responder information could potentially have some of the most powerful impact in the message, and some react as being impressed.

What if it were the other way around? My experience is that sometimes Prozac works, and when it does and it's the right drug, that's great. But sometimes Zoloft works, and in one person Zoloft works and Prozac doesn't. This tries to lead you to think to always use Prozac because it works much better with non-responders, and it's not an accurate representation. (PSYCH)

I'm highly suspicious of that being an objective study. Are they giving comparable doses? This almost reduces the believability about the whole thing, unless they want to give me some specifics about what the doses were in the study. (PSYCH)

Information about Prozac's tolerability and safety in overdose and in combination with other therapies is considered true, although not entirely unique.

Prozac is generally well tolerated at all indicated doses Prozac has been proven safe in overdose Clinical experience has shown that Prozac can be safely augmented

Psychiatrists generally feel that Prozac is well tolerated at the indicated doses for most patients, although some cannot tolerate high doses. PSYCHs agree that Prozac is safe in overdose, but indicate that this is also true of other SSRIs. Similarly, most psychiatrists are aware that Prozac can be safely augmented and that this is true of other SSRIs as well.

Higher doses can cause more side effects. It is not well tolerated in people who can't tolerate a higher dose and get side effects from higher doses. (PSYCH)

It is true that Prozac is safe in overdose; it's true of the others as well. (PSYCH)

I have augmented Prozac with other agents, so this fits with my clinical experience. I am not sure this makes it unique, though. (PSYCH)

Some PSYCHs object to perceived niching of Prozac for women.

v Female depressed patients often present with fatigue and lack of motivation, and some may also have special risks and comorbidities.

Many PSYCHs indicate that they are uncomfortable singling women out as the patients who most often present with fatigue and lack of motivation. They assert that their male patients can also present with these symptoms. However, when this phrase is removed from the message, PSYCHs seem less inclined to question the introduction to the female-patient portion of the message. Most PSYCHs think of pregnancy when they read the line regarding special risks and comorbidities.

I don't know if it's the 'often' part, any more often than men are. Both present…men can present that way, too. Maybe a few more women do, if I think about it, but I don't know about the 'often' part. (PSYCH)

I don't know about that statement. I think male patients also often present fatigue and lack of motivation. I'm not sure that female depressed patients have to show fatigue and lack of motivation more often. (PSYCH)

PSYCHs view the pregnancy database as additional support of Prozac's safety.

Prozac has the largest antidepressant safety database in pregnancy, which provides reassurance for those female patients who may have unplanned pregnancies

PSYCHs find the pregnancy database information to be believable, given its size of more than 2000. However, the majority interpret it more as additional evidence of Prozac's overall safety rather than a reason to prescribe it specifically for pregnant women.

One thing I think that has some validity is its use in pregnancy. It does have an extensive database for pregnant patients, in terms of information regarding the number of women who have taken Prozac during pregnancy. If I need to have a woman on antidepressants, I will, if possible, use Prozac for that reason. It's likely that the other drugs will turn out to be just as safe, but we just don't have the numbers. Yet it's also true that each of the SSRIs are different, so you can't just make an extrapolation that they are the same. By sheer numbers, that's one of the advantages of Prozac, this amount of study and data – it's all clinically relevant. (PSYCH)

It's helpful in reassuring patients, more than anything females that want to get pregnant at some point and worry what will happen if they get pregnant while on Prozac. (PSYCH)

Similarly to PCPs, PSYCHs find the PMDD information compelling; they are less impressed with the bulimia indication.

> Prozac has been shown to treat both the mood (irritability and dysphoria) and physical symptoms (breast tenderness, bloating) of Premenstrual Dysphoric Disorder and is the only drug approved for this indication by the FDA
> Prozac has been proven to reduce both binge eating and vomiting associated with bulimia and is the only agent approved by the FDA for this indication
> Prozac is also indicated for OCD

The information regarding the physical symptoms of PMDD is new to most PSYCHs and attracts their attention, some even claiming that this would convince them to increase their usage of Prozac in women. However, the point raises questions about dosing and which specific mechanism of action alleviates the physical symptoms.

> *I did not know this. Does this mean women have to take it all the time to see this benefit or can they take it intermittently? (PSYCH)*

> *I don't think I was aware of the fact that it improves the physical symptoms. That's what stands out to me. It's interesting. I'm wondering what the mechanism is for that. Curious as to how it works, why it does that. (PSYCH)*

Most PSYCHs say that they are already using Prozac in bulimia and OCD, so any mention of these conditions as FDA-approved merely supports their own impressions. However, FDA approval does not seem to influence PSYCHs' prescribing behavior, since so much of their prescribing is off-label.

> *An FDA approval alone does not make it the only option for me. (PSYCH)*

> *I know that what drugs get approved by the FDA has a lot to do with the fact that the company decides it wants to put its money into researching. So it may well be true, but other SSRIs could probably get these indications, too, if they wanted to pursue that. (PSYCH)*

The elderly information about formal FDA approval and lack of renal accumulation leads many PSYCHs to consider making Prozac the drug of choice for this population.

- Prozac is proven safe and effective in geriatric depression, the only antidepressant with formal FDA approval for these patients
  - As all patients get older, their renal function declines. Unlike other antidepressants, Prozac does not accumulate and does not lead to increased side effects in the elderly.
  - Prozac improves the quality of life including emotional and physical well being in elderly depressed patients.

Most PSYCHs are surprised that Prozac is formally indicated for geriatric depression. This new information, coupled with the lack of renal accumulation, motivates them to consider using the agent in elderly patients with renal impairment, although they indicate that they would first like to see the data.

> *I didn't realize it's the only antidepressant with formal FDA approval for geriatric depression. (PSYCH)*

> *Geriatric depression is new information to me. That would make me think strongly about using Prozac, if that were true, in patients who had significant renal impairment. I'd like to see that study in more detail. But that might be a benefit that Prozac legitimately has that the others don't have that would influence me to consider using in the elderly. (PSYCH)*

For the majority of physicians, the non-accumulation data enhances the overall perception of Prozac's safety; however, this information is counter-intuitive to many.

Some of their enthusiasm toward the geriatric indication is tempered by concern about Prozac's long half-life and potential interaction with other medications. Therefore, many would like to see information about interactions and the P450 pathway, as well as data about which other drugs the studied patients were taking.

While I'm sure it's true that Prozac was safe and well tolerated, my clinical experience says that would be with careful monitoring. It will take some time before the effects of it are seen, compared to some of the antidepressants with a short half-life; you have to keep an eye out for that over a longer period of time is a little more cautious. (PSYCH)

It's a problem if patients are taking other medications, and that's not included here and that is a big problem. You can get into big trouble if the other medication has P450 enzyme conflicts. (PSYCH)

It's the old problem with multiple medications. I'd like to see the P450 enzyme problem with patients. Which drugs are you talking about and what drugs are interacting? Prozac interacts with several drugs that are problematic: it increases or decreases the efficacy of those other drugs. So it's a more complicated drug to use in elderly patients. (PSYCH)

PSYCHs readily accept the co-morbid condition safety data; however, this information does not directly motivate them to project new prescriptions.

Prozac is the most studied antidepressant in depressed patients with concurrent medical conditions such as diabetes, post-MI, cancer, and HIV.

- Prozac was effective at relieving depression in these patients
- Prozac was shown to be safe and well tolerated in these often-debilitated patients on multiple medications.

PSYCHs also agree that Prozac is the most studied antidepressant because it has been around for the longest time. Therefore, they are generally willing to accept the claim that it can be used safely in patients with diabetes, post-MI, cancer and HIV.

Use in concurrent medical conditions is probably true, probably a function of how long it's been on the market. It's old news. I believe it is effective; it's nothing new. (PSYCH)

I accept that it can be used in concurrent medical conditions. The others could be effective in relieving depression, too. (PSYCH)

PSYCHs appreciate Prozac's multiple dosage strengths and formulations.

> Prozac has the flexibility to start at 10 mg in the elderly
>
> Prozac is available in several dosage forms, including 10 mg scored tablets, 20mg and 40 mg capsules, and even a liquid formulation

PSYCHs appear to appreciate the 10 mg scored tablets, spontaneously mentioning that they have some patients cut the tablet in half. They typically use this low dose in people who may be sensitive to medications or in anyone for whom a lower dose is optimal, such as children or the elderly. It appears that the availability of a 40 mg tablet is not widely known or remembered, but they admit that diversity of dosage-strengths/formulations increases flexibility. The liquid formulation is praised as ideal for the elderly and for people with swallowing difficulties.

I start with the 10 mg in anybody who I think might be sensitive to medications: likely to have side effects or anything. I forgot about the 40 mg capsules. (PSYCH)

I did not know about the 40 mg dose. The tens are scored so they are good for children and adolescents as well as the elderly. (PSYCH)

Many psychiatrists already do discuss Prozac as a treatment option with their patients because it is an efficacious anti-depressant.

> Given Prozac's power and versatility, would you consider discussing Prozac as a treatment option for your complex depressed patients who are partial and non-responders, female with special risks, or elderly?

Psychiatrists report that they have always considered Prozac in the patients discussed and that they find Prozac to be a good antidepressant.

I always consider Prozac in this particular subgroup. And I like Prozac. I like it. It's a great drug. (PSYCH)

EXHIBIT 22

Eli Lilly & Company

Cymbalta

For The Treatment of Major Depressive Disorder

U.S. Strategic Pricing Study

Exploratory Qualitative Market Research
Conducted With Payers, Physicians, and Patients

Presented By
Roberta Miller and Associates
August 2, 2002

Table of Contents

Study Objectives
PAYERS

- Identify specific contracting strategies currently employed with the antidepressant class; assess opinions regarding contracting strategies
- Identify economic obstacles which could possibly impede the addition of Cymbalta to formulary
- Determine currently formularies for antidepressants, restrictions, rationale of any management of SSRIs versus SNRIs, and recent changes to antidepressant formularies
- Explore assessment of current Cymbalta product profile
- Determine formulary status reaction with contracting at various price points

Study Objectives
PHYSICIANS

- Understand physicians' perceptions of cost and availability of currently marketed antidepressants
- Understand how physicians' perceptions of cost (as they define and think about cost) impact their prescribing behavior
- Identify key elements that shape physician perceptions of cost and availability
- Determine frequency and degree of influence of each such element
- Identify product attributes/ perceived benefits physicians feel justify cost premium

Study Objectives
PATIENTS

- Understand the context in which patients view cost and out of pocket expense (absolute dollars or incremental dollars over alternatives)
- Understand how patient cost affects behavior, both in terms of first prescription and subsequent refills
- Understand frequency and likelihood of pharmacy intervention
- Identify frequency of sample use prior to incurring out of pocket expense
- Understand role of out of pocket cost in making decision to fill either the first prescription or deciding to refill

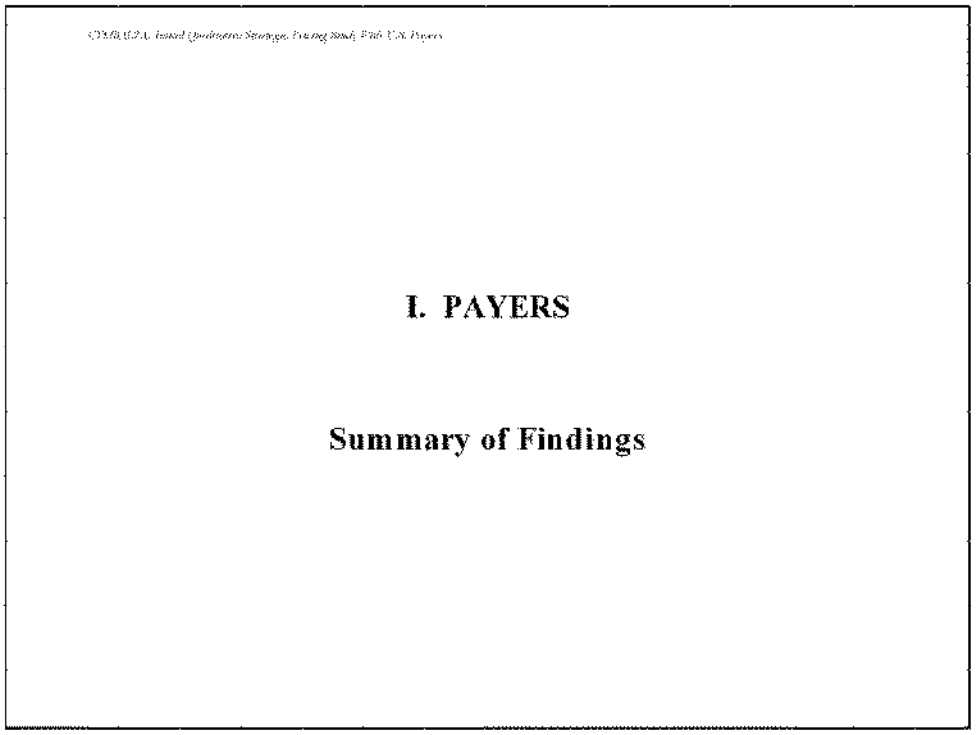
Strategic Business Decisions
The Research Study Will Support

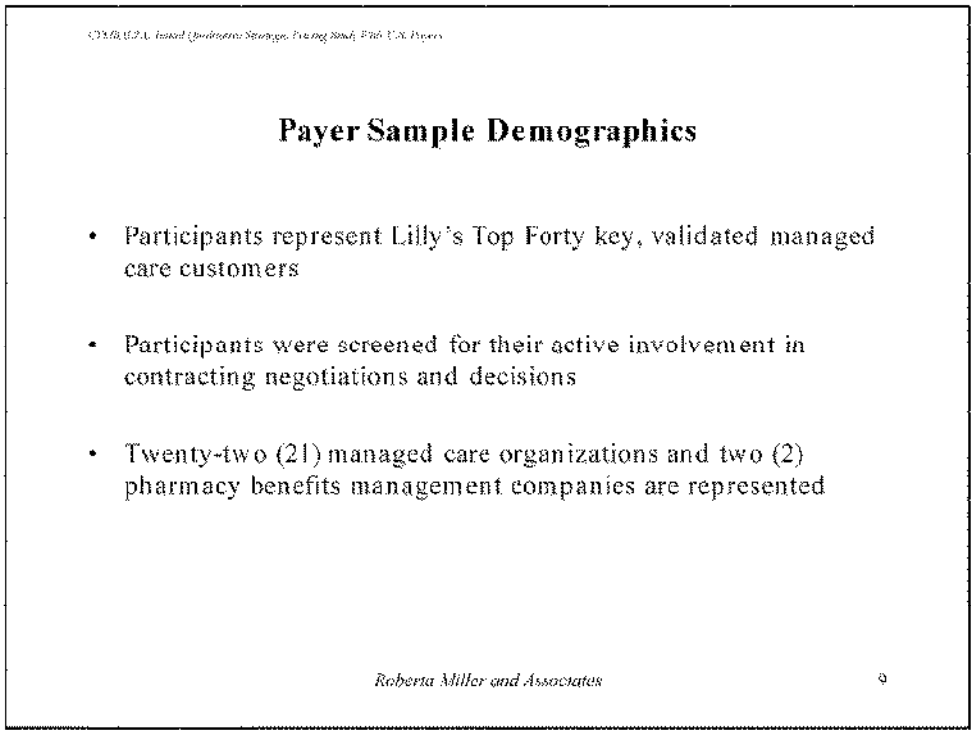
- Findings from this qualitative study will support a determination of list price strategy and rebate strategy for Cymbalta.

- **Findings born out of this market research study need to be viewed and evaluated in the collective context of the totality of qualitative and quantitative studies undertaken to support price and rebate strategy determinations for Cymbalta.**

Methodology and Sample

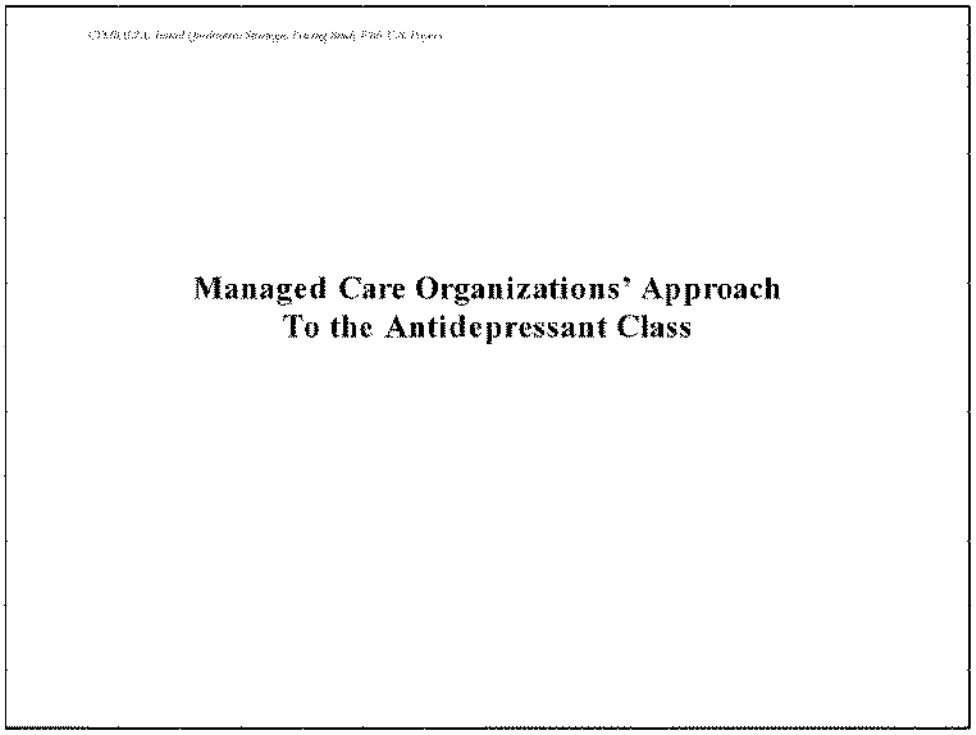
Interviewee	Interview Type	Sub-Groups	# Interviewed
Payers	Individual Phone Interviews	Pharmacy Directors	21
		Medical Directors	2
Physicians	Focus Groups	Specialists (Psychiatrists)	24
		PCPs	23
Patients	1:1 Interviews	Females	19
		Males	3





Plan Demographics
Pharmacy Benefit Design

• Three Tier	N=14
• Closed, Two Tier	N=3
• Open, Two Tier	N=2
• Open, Flat Co-Pay	N=2
• Closed, Flat Co-Pay	N=1
• Four Tier (Tier 3=50% co-pay, Tier Four=Nonformulary)	N=1



The Managed Care' View of Antidepressants

- Managed care organizations continue to view antidepressants as an important, yet very costly, therapeutic class.
- Antidepressants remain among the top five classes in terms of overall drug expenditure for all health plans surveyed.
- Most organizations maintain fairly open formularies because they understand the need for and importance of therapeutic options for this complex disease state as well as the highly individualized nature of patient' response.

How Antidepressants Are Reviewed

- Most managed care organizations (two-thirds) view and review the antidepressants as two distinct subgroups:
  - SSRIs
  - All Other Newer Agents (Non-TCAs, AKA "Atypicals")
  - However, one-third of health plans interviewed do view and review the antidepressants as one broad therapeutic class.

Recent Changes Within the Antidepressant Class

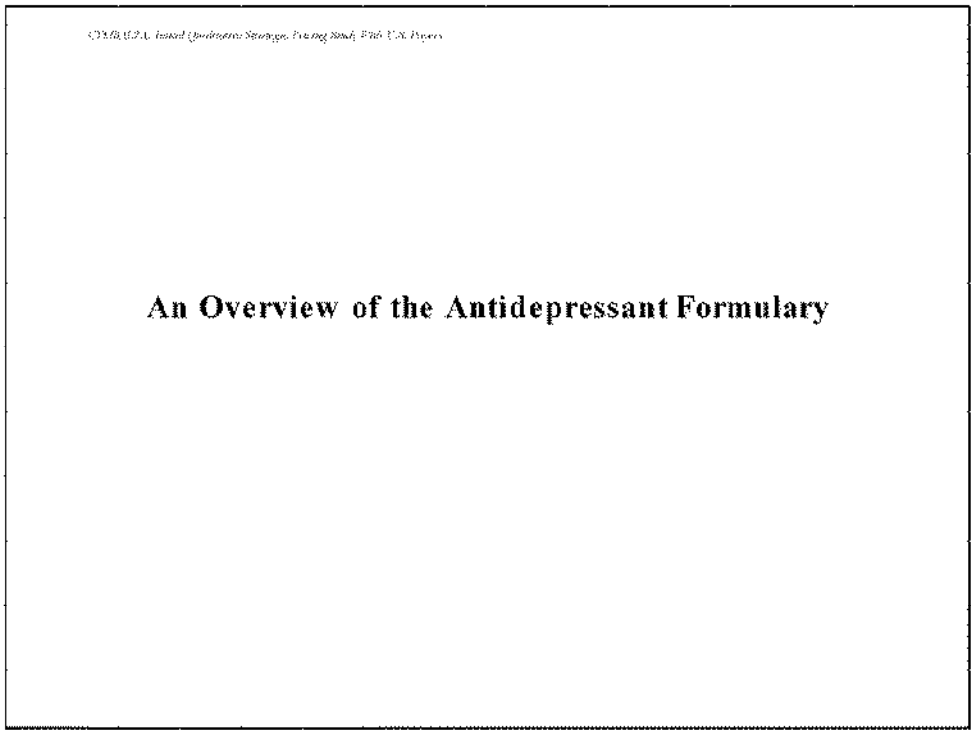
- Changes in market dynamics, new entries, and contracting opportunities are what spur non-annually scheduled reviews.
- The two most recent changes within the antidepressant class have been the introduction of generic Fluoxetine and the movement of Prozac to tier three/ nonformulary and the introduction of Paxil CR, which has been reviewed by half of the represented plans (only half of those chose to add the product to formulary.)
  - While the vast majority of plans have conducted a full class review of the antidepressants within the last year, some plans (6 of 23) have not reviewed the totality of the class within the last two years.

Anticipated Changes to the Antidepressant Class
No Actions Taken to Plan for Anticipated Events

- Most health plans know that both patent expirations and new product introductions are likely to occur in the antidepressant class over the next two years; however, they are not taking any actions in anticipation of these events.
  - Almost all know Lexapro will be introduced
  - Some, though less than half, are aware of Duloxetine, though Lilly's product is rarely identified by name
  - Most anticipate patent expirations for Paxil, Zoloft, and Celexa; all are uncertain when they will occur and acknowledge, unaided, that such changes in market dynamics could be significantly delayed by legal actions on the part of the respective manufacturers.

Anticipated Changes to the Antidepressant Class
No Actions Taken to Plan for Anticipated Events

- Health plans are not undertaking strategies to prepare for these changes in market dynamics; most are very focused on the current implications of generic Fluoxetine's entry and trends related to its uptake.
  - A few plans are currently exploring the feasibility of taking action (formulary changes, restrictions, academic detailing) to promote the use of generic Fluoxetine first line for all new starts.



The Antidepressant Class: A High Degree of Coverage and Availability

- Health plans surveyed are not exerting a high degree of formulary control over the antidepressant class, with the exception of Remeron and Serzone.
- Effexor / XR is on formulary/ tier two among all plans surveyed.
  - Only one plan has any type of restriction specific to Effexor's utilization, limiting tier two coverage to psychiatrist' use only.
- The vast majority of plans have all three branded SSRIs discussed - Paxil, Zoloft, and Celexa - available on formulary/ tier two.

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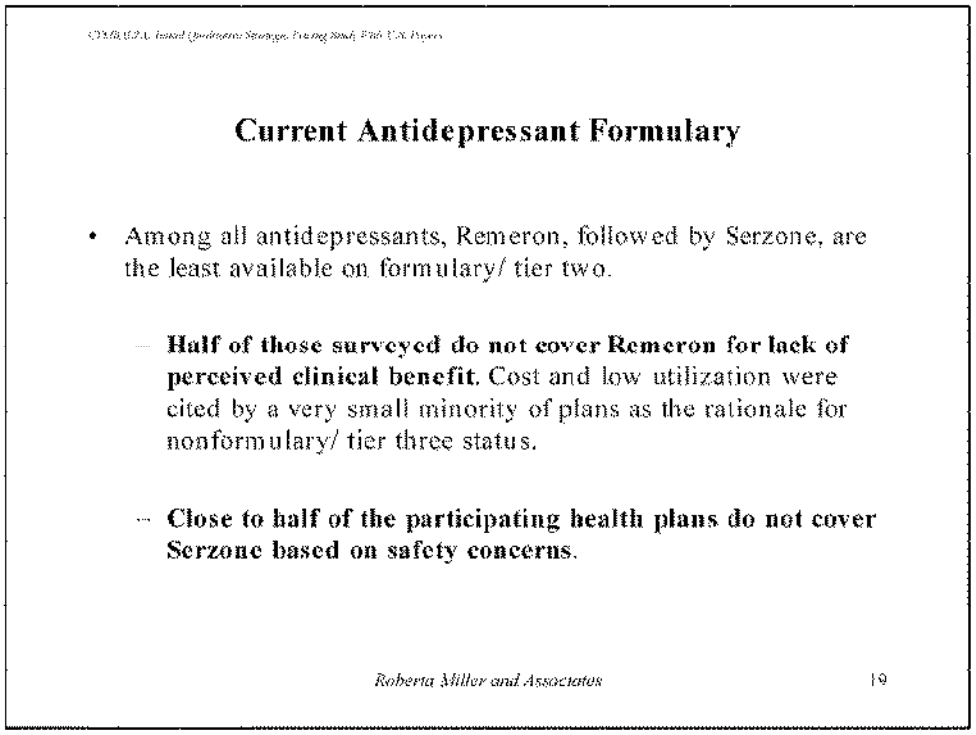


Current Antidepressant Formulary

- Of the twenty-three (23) organizations surveyed:
  - Four **(4) do not cover Celexa** because of exclusivity clauses/ potential loss of market share incentive rebates with other SSRI manufacturers.
  - Three **(3) do not cover Zoloft** because of contracting issues with Pfizer.
  - Two **(2) do not cover Paxil** because of a perceived lack of cost effectiveness (efficacy, side effects, cost).
  - **Paxil CR is nonformulary/tier three in over half (14 of 23).** Seven plans have not reviewed Paxil CR; five see the product as a patent gimmick without clinical merit; two do not currently have Paxil on formulary.
  - **Wellbutrin SR is nonformulary/tier three within two plans** because of inappropriate utilization for smoking cessation.

Restrictions on Antidepressants

- The majority of plans surveyed do not employ any restrictive action for the antidepressant class.
- The most common restriction on the antidepressants is a tablet splitting program. This restriction is implemented by seven of the twenty-three participating organizations (7 of 23).
  - Three plans institute quantity level restrictions for all antidepressants, also referred to as dose optimization, in which specific dosage strengths are not covered.
  - Three plans implement quantity limits of thirty per Rx.
  - Three require prior authorization of Wellbutrin SR for depression use only; one plan restricts Effexor/ XR and Wellbutrin SR, first line, to specialist' use only.

Early Reviews of Antidepressants

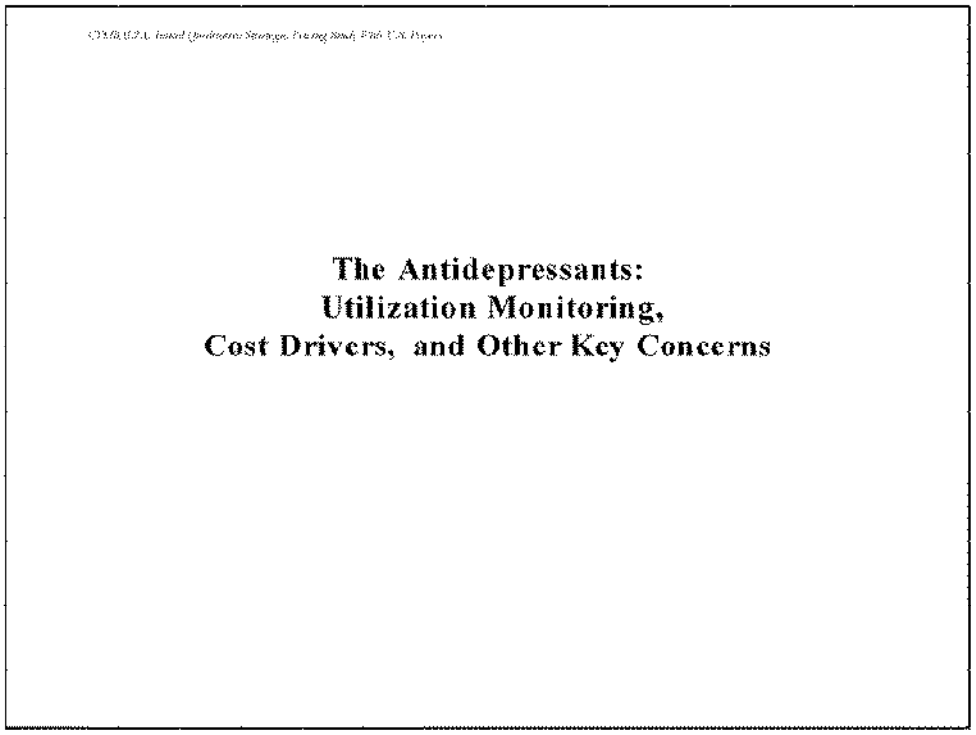
- Antidepressants, with the exception of the initial introduction of Prozac and the advent of the SSRI class, are rarely, if ever reviewed in a faster-than-normative time line.
- For some plans that time line is two to four months; however, for many organizations, the time line for formulary review is a minimum of six months.
- Anti-infectives, chemotherapy agents, MS drugs and HIV therapies are categories most likely to receive the fastest formulary reviews.

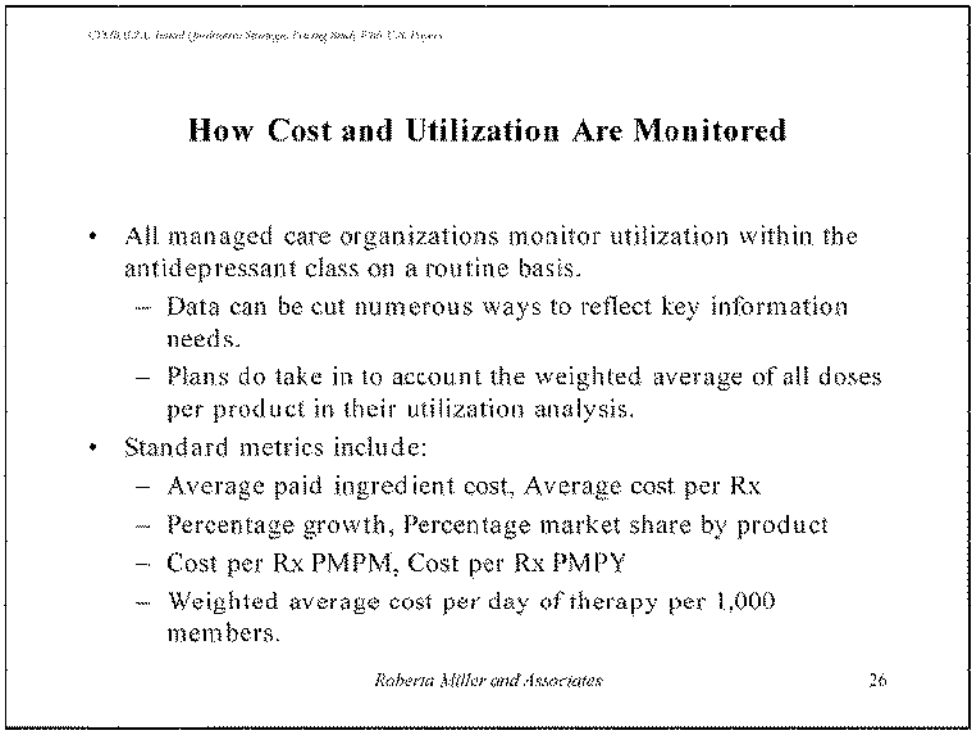
Early Reviews of Antidepressants

- Exceptions to this review timeline for antidepressants are rare and would include:
  - One plan reviewed Prozac Weekly within its first two months post-launch because its introduction prompted a re-assessment of the Lilly contract.
  - One plan reviewed Celexa in its first three months to take advantage of a compelling, early acceptance rebate incentive.
  - Future introductions of breakthrough products on the order of Prozac.

Formulary Status: Definitions for Nonformulary, Tier Three, Exclusion

- "Off-formulary" is defined by Pharmacy Directors as nonformulary or tier three.
- For three tier lives, a product that is not added to formulary is automatically placed on the third tier.
- For closed formulary lives, a product that is not added to formulary is automatically nonformulary, and available only through a medical exception approval process.
- Exclusions are products or therapeutic classes that are excluded from benefit design, meaning they are not available, not covered, and for which no medical exceptions are made.



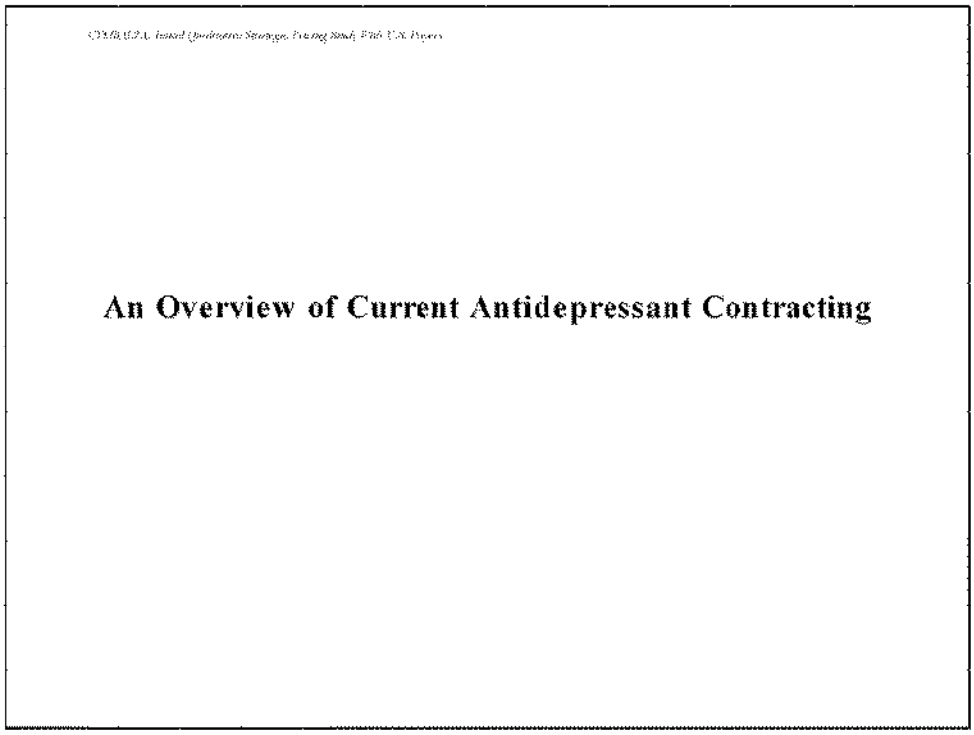


Cost Drivers: Weighted Dose Distribution, QD/BID Dosing

- Most health plans are not *routinely* assessing whether or not the weighted dose distribution and/ or QD versus BID dosing are having a significant impact on net cost.
- Among plans that have examined this issue, a few different perspectives emerge:
  - This is a recognized issue and the plan has quantity level limits, quantity edits, and/ or tablet splitting restrictions to address it
  - Dose titration is viewed as a necessary component of some antidepressant therapy and the plan is not focused on it
  - There is an acknowledgement among a small number of plans of high dose utilization of Effexor (N=5) impacting net cost, but Effexor is not a high cost/ utilization driver, so no action is taken
  - Wellbutrin SR is cited for dose escalation and BID dosing (N=2), again, no action is being taken because it is not a cost driver.

Most Significant Concerns Regarding the Antidepressant Class *Cost, Compliance, and Outcomes*

- Cost, Compliance and Health Outcomes continue to dominate as the top three most significant concerns regarding the antidepressant class.
- Antidepressants remain in the top five most expensive drug expenditure categories among all organizations surveyed.
- Health plans remain uncertain as to the actual long term value of antidepressant therapy and fear that many, if not most, patients are not staying on medication long enough to achieve and sustain optimal therapeutic outcomes.



Current Contracts for the Antidepressant Class: What Managed Care Finds Most Appealing *Flat Access Rebates with Market Share Incentives*

- Flat access rebates with market share incentives (often tiered incentives), are by far, the most preferred contract type; however, there are some organizations that prefer a flat access rebate without any market share incentives for the antidepressant class.
  - Pharmacy Directors emphasize that a rebate has to at least equal the loss of member co-payment dollars lost when a product is moved from tier three to tier two.

Current Contracts for the Antidepressant Class: What Managed Care Finds Most Appealing *Low List Price, Minimal Rebating*

- All organizations prefer a low list price and minimal rebating versus a higher list price and moderate rebating:
  - Health plans prefer to have their money up front (time/ value/ $)
  - MCOs believe rebates send a negative message to physicians and members regarding the business relationship between MCOs and Pharma
  - Most do not like the administrative burden of monitoring any level of rebates.

Current Contracts for the Antidepressant Class: What Managed Care Finds Least Appealing
Bundling

- Any type of bundling agreement is viewed by all managed care decision makers as the least appealing contract type because it does not allow for individual clinical determinations for each given product.
  - Managed care views bundled agreements as a forced acceptance of products they may view as clinically inferior, overpriced relative to clinical value, or a "me-too."
- Contracts with particularly restrictive language are also very unappealing:
  - Terms that disallow for contract re-negotiation during the contract period
  - Requirements regarding co-payment ceilings for a given tier.

Current Contracts for the Antidepressant Class: What Managed Care Finds Least Appealing
Bundling

- While many plans find what they refer to as "preference" agreements (AKA as exclusivity contracts) acceptable, a few plans do not like and will not accept contracts with terms that specify that a product can only be one of two or one of three on formulary for a given class or designated product grouping.

An Overview of Current Contracts Within the Antidepressant Class *Pfizer and GSK*

- Most current contracts for the antidepressant class are access-driven with tiered market share incentives.
- Pfizer, and to a lesser degree GSK, continue to have a significant number of bundled contracts and typically require some level of exclusivity within the SSRI class. Some, though not many exclusivity contracts, (referred to by plans as preference agreements) do include Effexor/ XR and Wellbutrin in the formulary product mix.
  - Products are most often not identified specifically
  - Exclusivity for this class is typically defined as one of two or one of three in whatever basket the pharmaceutical company has specified (all branded SSRIs, SSRIs and Effexor, etc.)

An Overview of Current Contracts Within the Antidepressant Class
Wyeth-Ayerst

- Less was recalled, top of mind, regarding the specifics of Wyeth's contracts, in large part because Effexor represents far less drug expenditure for health plans than do the SSRIs.
- Those that could recall specifics state that Wyeth's contract for Effexor/ XR is access-driven, although it appears Effexor/ XR is sometimes bundled with Premarin products.

An Overview of Current Contracts Within the Antidepressant Class
Wyeth-Ayerst

- A few complain that Wyeth's contracts are overly complicated in their terms and language.
- A few indicate that Wyeth requires some level of preference (exclusivity) within the atypical antidepressants, e.g., one of X among Wellbutrin SR, Serzone, Remeron, and Effexor.
  - One Pharmacy Director states that Wyeth is most interested in blocking the availability of Wellbutrin SR and negotiates their contract to this end.

An Overview of Current Contracts Within the Antidepressant Class
Forest

- The phrase "simple and straightforward" was used by numerous participants to describe Forest's contracting.
- Forest was also commended for its willingness to edit the terms of a contract as needed.
- Forest's contracts are access-based (where the plan gets a standard % rebate) and unbundled.

Antidepressant Manufacturers Perceived As Most Aggressive Pricing and Contracting

- Among respondents who believe an antidepressant manufacturer does stand out as most aggressive in its approach to pricing and contracting, Forest is viewed by managed care as the company with the most aggressive approach to pricing and contracting; however, many managed care decision makers feel none of these companies are distinctive or unique in terms of their pricing and contracting strategies.
  - One Pharmacy Director praised both Lilly and SmithKline (in the past) for the most aggressive contracting efforts.

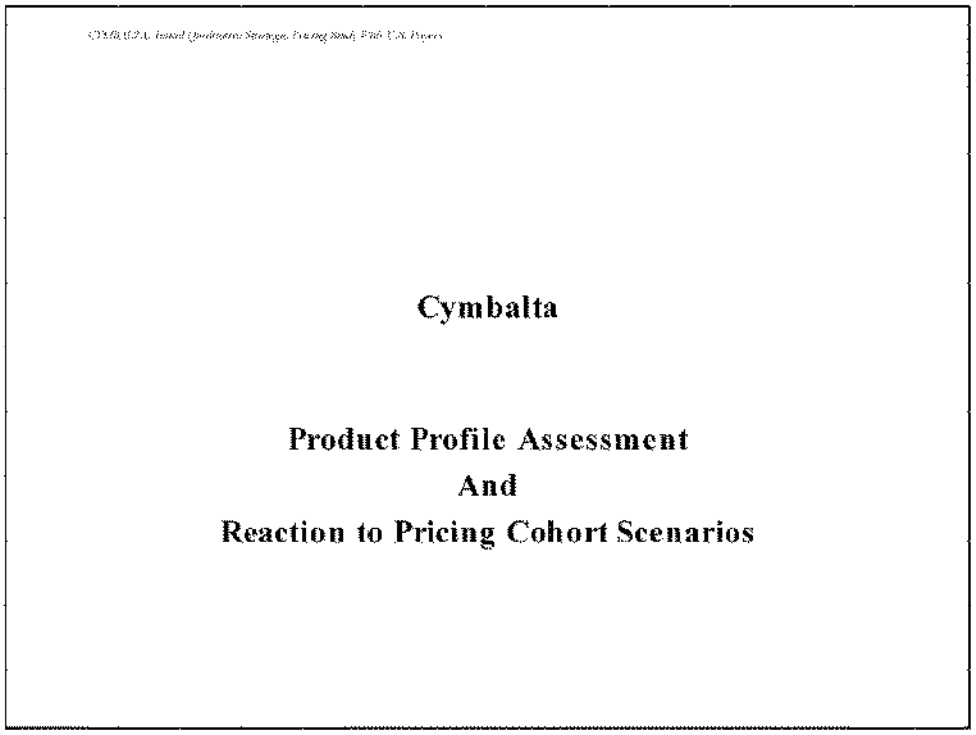
An Overview of Current Contracts Within the Antidepressant Class *Market Share Contracts*

- Among plans represented, for market share contracts, the geography used to calculate market share is either the plan alone or against national performance. Plans appear comfortable without whatever geography (plan or national) is being used for their given contracts.

- Market share agreements can be calculated numerous ways.
  - Percent of market share of all SSRIs is the most common market basket for calculation, though the market basket could, and sometimes does, include other products, such as Effexor/ XR and Wellbutrin SR.
  - None of the contracts, among any of these plans, offer high dose protection for any antidepressants.

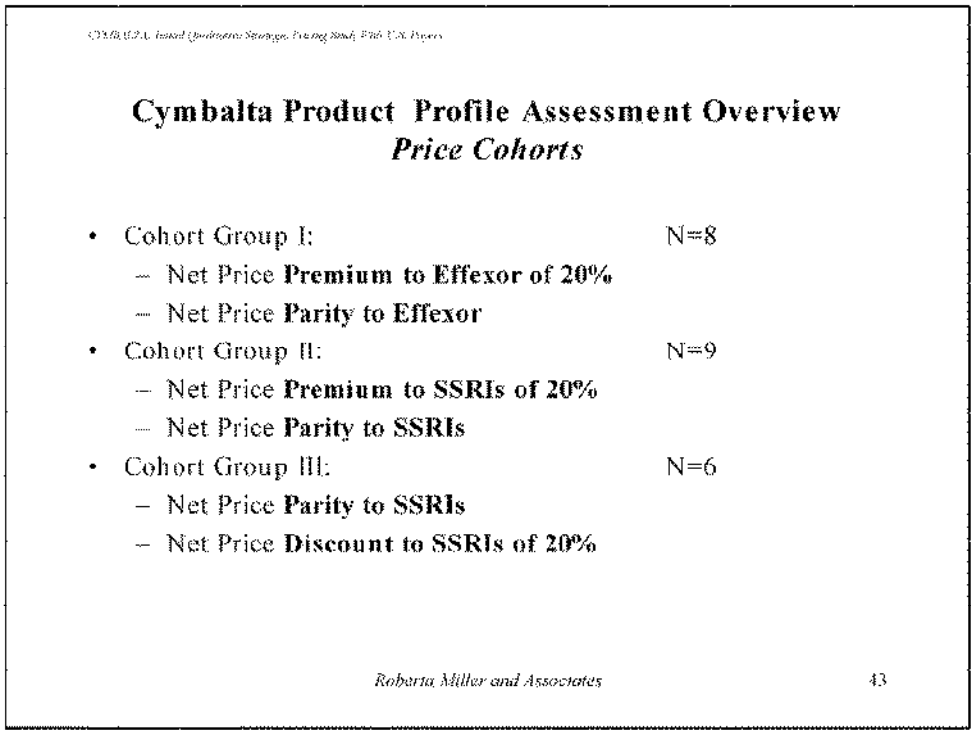
No Contract Impediments Exist To Hinder the Addition of Cymbalta

- None of the managed care organizations surveyed have any existing contract restrictions that would preclude the addition of Cymbalta to formulary.



Cymbalta Product Profile Assessment Overview
Methodology

- Participants were faxed a current, two-page Cymbalta product profile in advance of the interview and were asked not to read the information until so requested by the interviewer.
- After reviewing the profile during the telephone interview, participants were divided in to three cohort groups to explore reaction to formulary status with contracting at specific price points. Two set price points were provided for each group.
- If the respondent asserted that the product would not be added to formulary at either price point, participants were then asked, unaided, to determine where the product would need to be priced from a net price per day to be added to formulary.



CYM-U.S.A. Initial Qualitative Strategic Pricing Study, Feb. U.S. Payers

Cymbalta Product Profile Assessment Overview
Price Cohorts

- Cohort Group I: N=8
  - Net Price **Premium to Effexor of 20%**
  - Net Price **Parity to Effexor**
- Cohort Group II: N=9
  - Net Price **Premium to SSRIs of 20%**
  - Net Price **Parity to SSRIs**
- Cohort Group III: N=6
  - Net Price **Parity to SSRIs**
  - Net Price **Discount to SSRIs of 20%**

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Cymbalta Product Profile Assessment
Looks Interesting, Lacks Clear Differentiation

- Many participants began their assessment of Cymbalta with the phrase "looks interesting;" however, very, very few went on to ascertain clear areas of differentiation or superiority.
- None, at first blush, without the clarity and emphasis of marketing and positioning, believe Cymbalta offers clear clinical advantage over the SSRIs or Effexor.

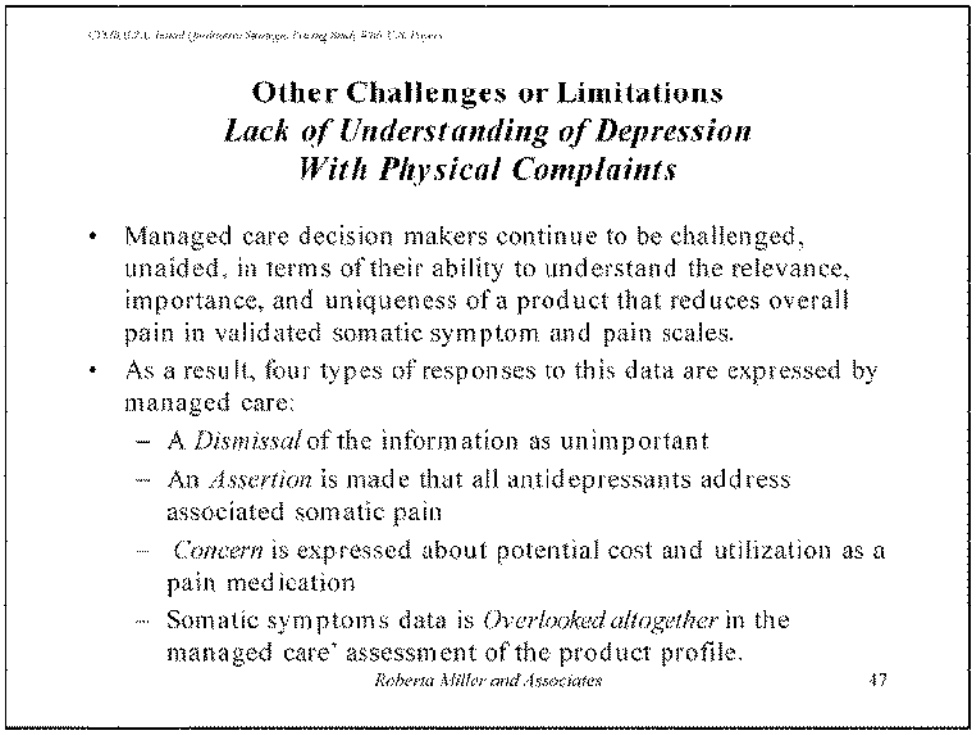
Challenges or Limitations Posed By the Product Profile Selected for this Research Study

- The fact that Cymbalta was studied at 80 mg and will be introduced at 30 mg and 60 mg was a major issue for payers.
- For many participants, the lack of onset, efficacy, safety, and remission, data, at dosage strengths that will be marketed, clearly weakened the overall presentation of clinical information.

Challenges or Limitations Posed By the Product Profile Selected for this Research Study

- While some applaud the fact that a head-to-head study was undertaken, several managed care decision makers question why the comparator is Paxil, rather than Effexor, and *why* Paxil 20 mg, which they view as a less than effective dosage strength.

- Additionally, some wording in the profile appeared to mute the overall significance of the information for some participants:
  - Phrases such as "were 112% more likely to achieve remission" were challenged for their clinical merit and statistical significance.



Key Product Comparators For Formulary Review
All Formulary Antidepressants and Effexor Specifically

- The vast majority of health plans (18 of 23) expect Cymbalta to be reviewed in relation to all formulary antidepressants - SSRIs and Atypicals.
  - The other five organizations anticipate the review focusing on clinical value in relation to only the Atypicals.
- Based upon its mechanism of action, the key product comparator will be Effexor.
- The introduction of Cymbalta will not prompt plans to view the SNRIs as a distinctive class.

Response to Pricing Scenarios

Cohort Group I: N=8
Cohort A: Net Price **Premium to Effexor of 20%**
Cohort B: Net Price **Parity to Effexor**

- None of the eight participants in this cohort group would expect Cymbalta to be added to formulary at any premium to Effexor.
- Without significant clinical superiority, which was not immediately evident to participants, none would expect Cymbalta to be added to formulary at net parity pricing to Effexor.
- Expectations for where Cymbalta would need to come in, from a net price per day, to be added to formulary, ranged from a 10% to a 40% net discount to Effexor; one Pharmacy Director indicated a 25% to 30% net discount to Celexa is needed.

Response to Pricing Scenarios

Cohort Group II: N=9
Cohort A: Net Price **Premium to SSRIs of 20%**
Cohort B: Net Price **Parity to SSRIs**

- None of the nine participants in this cohort group would expect Cymbalta to be added to formulary at any premium to the SSRIs.
- Four of nine definitively believe Cymbalta would be added at parity to the SSRIs. One additional respondent feels it would be added if parity priced to, specifically, Celexa.
- Among the other four respondents, expectations for where Cymbalta would need to come in, from a net price per day, to be added to formulary, ranged from 15% to 20% less than a clinically equivalent SSRI, to $2 per day, to some degree of price advantage relative to the least expensive SSRI.

Response to Pricing Scenarios

Cohort Group III: N=6
Cohort A: Net Price **Parity to SSRIs**
Cohort B: Net Price **Discount to SSRIs of 20%**

- One of the six participants in this cohort group would expect Cymbalta to be added to formulary at parity to the SSRIs. One other sees the product being added if net cost is equivalent to that of Celexa, specifically.
- An additional two respondents feel Cymbalta would be added at a 20% net discount to the SSRIs.
- Among the other two respondents, neither believes Cymbalta will be added to formulary/ placed in tier two, regardless of cost. One feels that product has no clear clinical advantage in a saturated market; the other states that the P&T Committee views all SNRIs as second-line (tier three) relative to the SSRIs.

Response to Cymbalta's Clinical Profile And Pricing Scenarios In Summary - The "Whys" Behind Responses

- The focus among managed care organizations currently is to seek methods to improve compliance and long term outcomes in the treatment of depression, and, to lower cost in a class that is consistently in the top five of drug expenditures.
  - Among health many plans, there is a pervasive perception that a lot of money and medication is being thrown at this disease state with relatively poor compliance and questionable long term outcomes.
  - Some plans are also turning their attention to trying to promote, either through step therapy guidelines or academic detailing, the use of generic Fluoxetine first line.
- In short, little initial enthusiasm exists for products not viewed as different or innovative.

Response to Cymbalta's Clinical Profile And Pricing Scenarios In Summary - The "Whys" Behind Responses

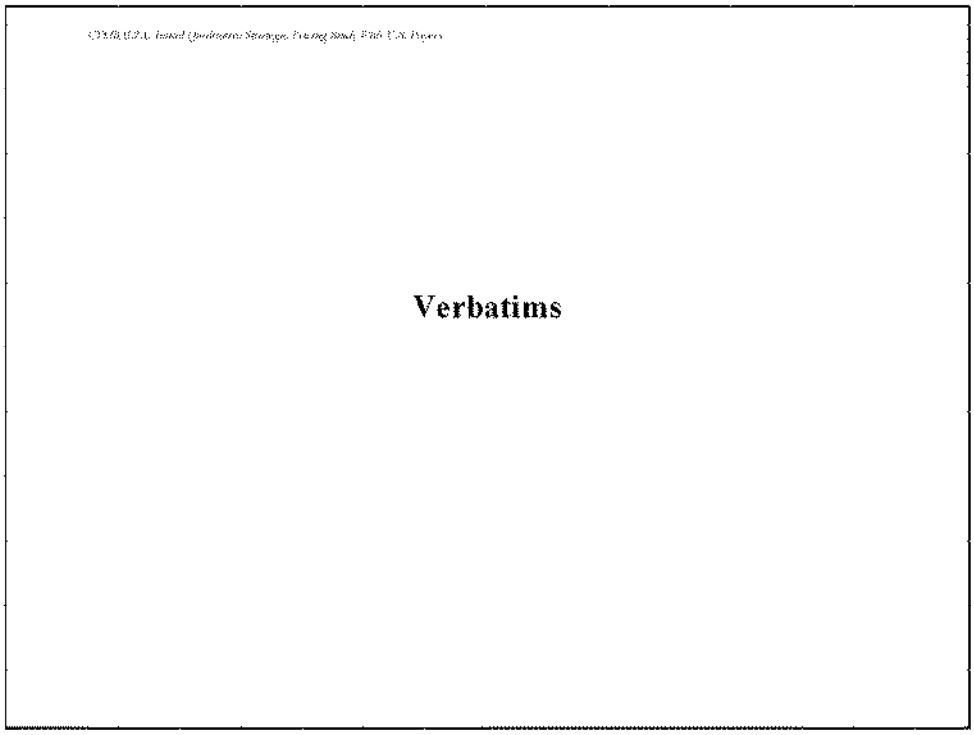
- While they recognize the importance of individualized treatment and the need for therapeutic options for depression, health plans can be very cautionary in their initial assessments of new products, particularly if they cite inconsistencies or perceived holes in the presentation of clinical information.

- Without the strength of a marketing and message campaign, this particular Cymbalta product profile did not stand up very well, on its own merits, for managed care decision makers.
  - As stated earlier, a few aspects of the profile left managed care very unclear as to the product's clinical value in a market that is perceived as saturated and in need of only novel, inexpensive, or clearly differentiated new agents.

Response to Cymbalta's Clinical Profile And Pricing Scenarios In Conclusion

- While only five of twenty-three participants state that they expect formulary acceptance at parity pricing to the SSRIs, the fact remains that with a strong positioning campaign, a directed educational effort regarding physical symptoms, and answers to consistently raised clinical questions, the formulary acceptance outlook for Cymbalta can be far more favorable.

- It is important to reflect upon the fact that Effexor is on formulary in all of the plans surveyed and that no existing contracts would impede the addition of Cymbalta.



Verbatims
An Assessment of Cymbalta, Reaction to Pricing Scenarios

- *"These findings are hard to evaluate; the presentation of the data really leads to a lot of important questions, particularly about what happened at 80 mg and higher doses of this drug and what will occur if physicians are prescribing a 30 mg with a 60 mg. What kind of side effects are we likely to see? I also have no idea how large some of these studies are... I think the comparator will be Effexor, so it seems strange that the head-to-head was against Paxil, but our review will evaluate this product against our total formulary for depression. At any premium to the SSRIs this product will not get added, especially with all of our safety concerns with new products. Our typical script, without rebate, is $93.85 for Effexor, compared to $76.41 for Paxil. At parity with our most cost-effective SSRI, it's a may-add, but only if there is a clear safety or efficacy advantage over Effexor."*

Verbatims
An Assessment of Cymbalta, Reaction to Pricing Scenarios

- *"The data compared to Paxil is interesting and the the reduction of symptoms in two weeks, if born out, is impressive, particularly if this improves compliance. I would have hoped for better anxiety scores and the physical symptoms piece is interesting, something I have just learned about recently. I question why there are not studies against Effexor, makes me unsure who is their competition or if there's some data being withheld because it isn't favorable. I don't honestly see any clear differentiation, so I think it will come down to cost unless you have a compelling compliance story. Without a study against Effexor, I don't think we would add this. At a twenty percent premium to Effexor, I don't think anyone will add it. Even at parity, we won't add it. Effexor is well established and has significant market share here, and this doesn't look to serve a new niche. I'd say you'd have to come in at close to a fifteen percent discount to Effexor."*

Verbatims
An Assessment of Cymbalta, Reaction to Pricing Scenarios

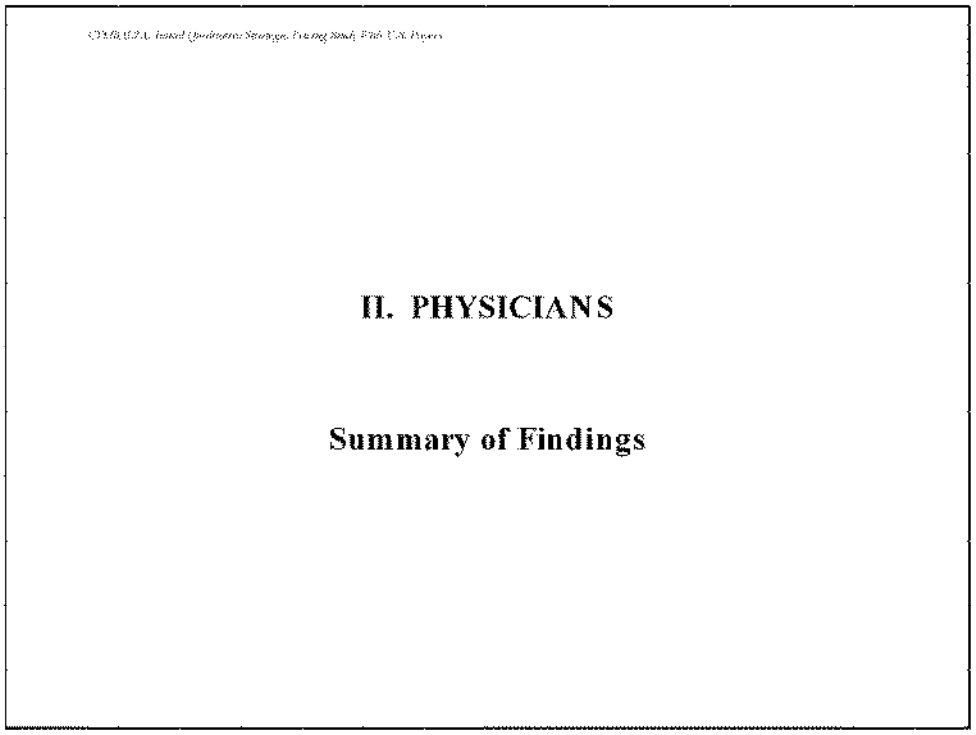
- *"This drug looks pretty good on paper in terms of its efficacy. My major concern is why it was studied at 80 mg and will be introduced at 30 mg and 60 mg - what did they see at 80 and what are the clinical findings at these lower doses? Looks like they've compared apples to oranges, given the dosing in the trials is not what will be marketed. And what dose are the side effects based upon? Given the comparison to Paxil, this product will be looked at against all SSRIs, but so far, I can't see anything clinically that sets it apart. At parity with the SSRIs - and that's a broad spectrum of cost to us - I would not see any reason to add this. It will sit in tier three for some time. At a twenty percent discount to the SSRIs, we will take a closer look, and then it becomes a may-add, but this profile leaves too many questions to be able to ascertain the formulary outcome."*

Verbatims
An Assessment of Cymbalta, Reaction to Pricing Scenarios

- *"Initially, I would say this product looks good. I like that it's a balanced, dual reuptake inhibitor and the remission numbers are substantial, and the side effect profile looks pretty good. The comparison to Paxil is good, as is the incidence of sexual dysfunction. My concerns are that it may be perceived as a heavy dose product, it sounds like two to three times the average dose for an antidepressant - how do you titrate and are there HAMD scores for 30 mg use and 60 mg use? The P & T Committee will also question whether we will see off label use for pain. The potential use for pain really bothers me. At a twenty percent premium to Effexor this is clearly a tier three product. The market is over-priced now. At parity, things don't look any more promising. It's a crowded field, so you will have to build some incentive in for managed care, twenty five to thirty percent below Celexa and we'll be interested."*

Verbatims
An Assessment of Cymbalta, Reaction to Pricing Scenarios

- *"The emphasis on pain reduction is unique, but the expansion of the pain category worries me. We don't need another Neurontin, but if it is effective in pain and less expensive than a product like that, that's a good thing. The comparison to Paxil 20 mg is weak. That is not an effective strength and I think Paxil is one of the weaker drugs, clinically, in this category, so I am not sure the comparison affords them much. The remission rates look interesting but what does "112% more likely" really mean; that's very vague. The dry mouth and nausea are a bit of a concern. We'll look at this relative to all antidepressants on our formulary. Right now, the pain piece could have some promise for differentiation but also some fear regarding utilization. We'd also like to see a comparison to Fluoxetine 20 mg or Zoloft 100 mg. At parity with SSRIs, we'd place it in the third tier and see what psychiatrist' use looks like. At $2/day, we'll take a look at the six-month mark. Given that our push right now is to get doctors to prescribe generic Fluoxetine first line, this drug won't get a lot of attention until a fair amount of clinical experience is established."*



Physician Sample Demographics

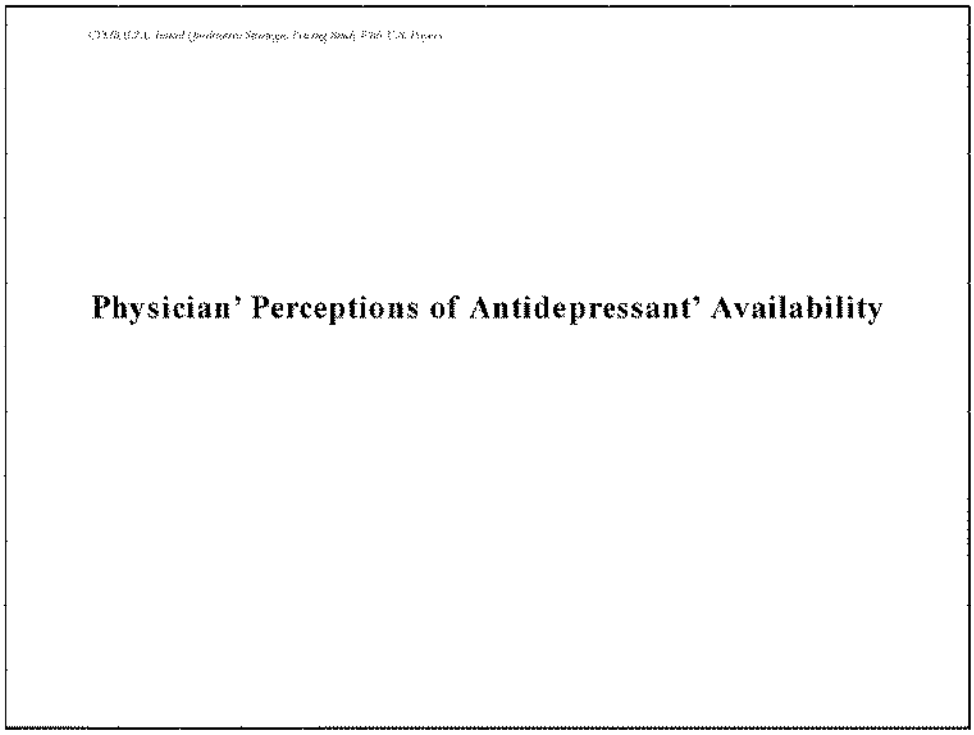
- Four major U.S. markets are represented in this qualitative strategic physician pricing research:
  - Atlanta
  - Philadelphia
  - Chicago
  - Los Angeles
- Focus groups were conducted with both Primary Care Physicians and Psychiatrists in each of the four markets.
- Physician research was fielded the week of June 24th - June 27th, 2002.

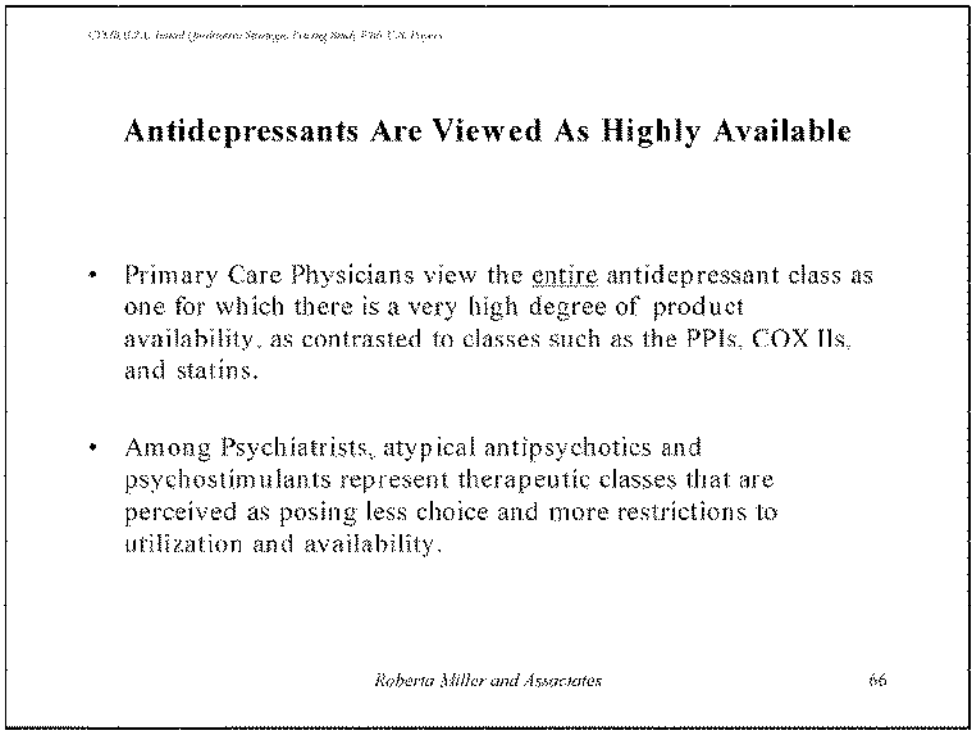
Physician Sample Demographics

- Primary Care Representation: N=23
  - Internal Medicine N=11
  - Family Practice N=11
  - General Practice N= 1
  - Six Primary Care Physicians from each of three markets, five from one market
- Psychiatrist Representation: N=24
  - Six Psychiatrists from each of four markets

Physician Criteria For Participation

- Primary Care Physicians and Psychiatrists
  - 1 - 30 years in practice
  - Age 30 to 65
  - >80% of time spent seeing patients in-office
  - Started or changed antidepressant therapy for >5 patients in last two weeks
  - No contract (advisory, clinical trial) with pharmaceutical manufacturers
  - No participation in antidepressant market research in past three months
  - Have seen two or more representatives within last month:
    - Forest, GSK, Lilly, Pfizer, Wyeth



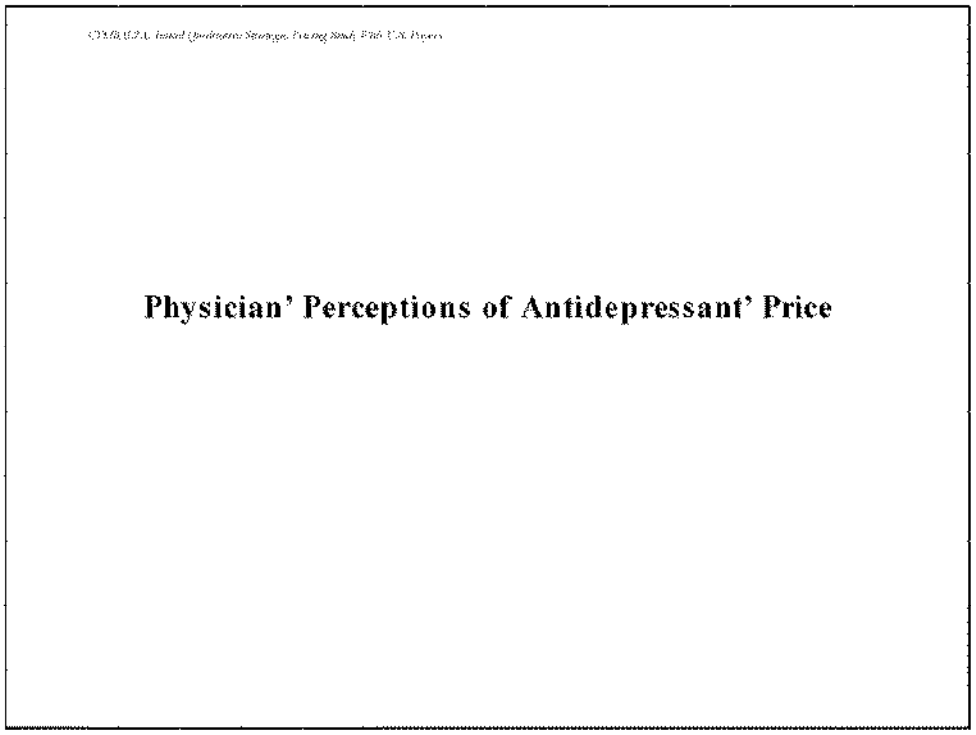


Availability Is Not Driving Antidepressant Prescribing Decisions

- Physicians feel they cannot keep up with the ongoing, myriad of changes to each local health plan's formulary.
- As a result, physicians make clinical determinations as to the optimal treatment of depression and deal with formulary availability issues as they come up.

Availability Is Not Driving Antidepressant Prescribing Decisions

- If a particular product is not available on a particular formulary, given the very individualized nature of antidepressant response, physicians will lobby a managed care organization for approval.
  - They also combat availability issues by generously providing samples, particularly for new starts, and economically challenged patients (indigent, Medicaid, working poor, Medicare.)



Lack of Knowledge Regarding Antidepressant Cost

- Primary Care Physicians and Psychiatrists were unable to clearly identify relative price, relative availability, or speak to an understanding of list price.
- Price - actual and relative - are simply not on the radar screen of importance to physicians.

Lack of Knowledge Regarding Antidepressant Cost

- Both Primary Care Physicians and Psychiatrists lack knowledge of pharmaceutical product' cost and are uncomfortable even engaging in drug cost discussions because of their lack of expertise and information in this arena.
  - Price is not driving prescribing decisions for antidepressants.

How Physicians Define and Think About Antidepressant Cost
What The Patient Pays

- Physicians define and think about antidepressant cost, first and foremost, in terms of anecdotal payment information received from patients, often expressed as complaints about patients' out-of-pocket expense, "Do you know how much this drug cost me?" or, " My co-payment for this product was X and I usually only have to pay Y!"

Lack of Knowledge Regarding Antidepressant Cost
List Price and Most/Least Expensive Antidepressant

- Physicians' lack of price knowledge is no more evident than in two exercises they completed during each focus group.
- First, they were asked to define "list price."
- Then, physicians attempted, individually, to arrange four antidepressants in order from the most to the least expensive: Paxil, Zoloft, Celexa, Effexor XR.
- There was absolutely no consensus in response to either question, nor was there a high degree of comfort that their assertions were anything but mere guesswork.

Lack of Knowledge Regarding Antidepressant Cost
Definitions of List Price

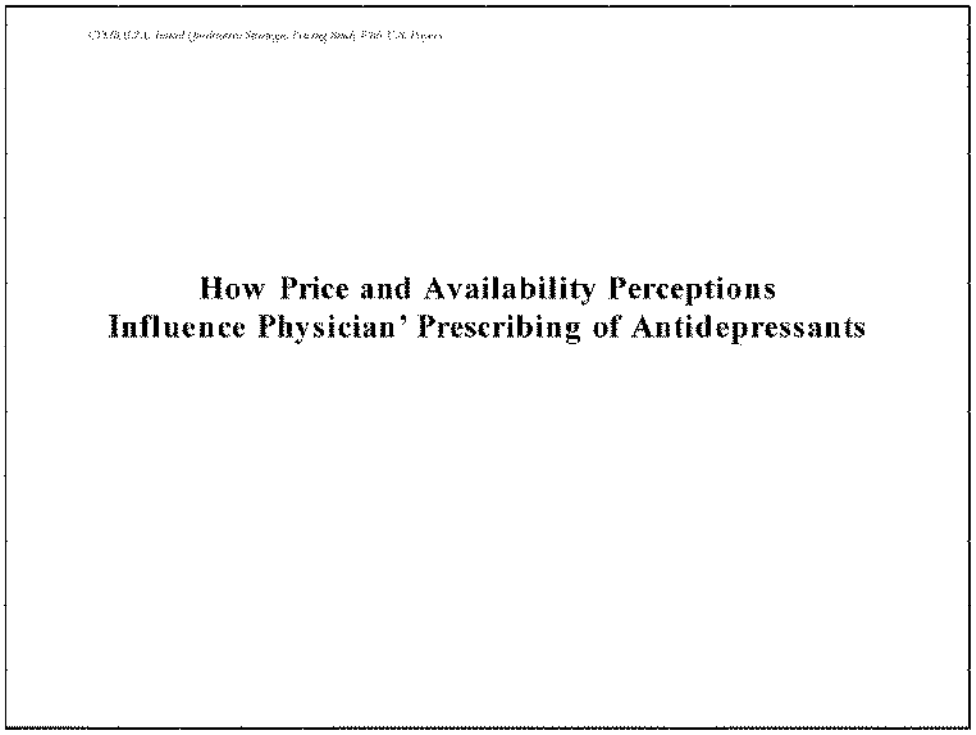
- Physician' definitions of "list price" include the following:
  - Retail price
  - Average wholesale price
  - Wholesale price
  - Price a pharmacy pays for a drug
  - Price a patient pays out-of-pocket for a drug
  - Price per unit
  - Price per month supply
  - Sticker price
  - Manufacturer's price

Lack of Knowledge Regarding Antidepressant Cost
No Consensus in Perceptions of Most and Least Expensive Antidepressant

- Each of the four products - Paxil, Zoloft, Celexa and Effexor XR - is perceived by some segment of Primary Care Physicians and Psychiatrists as both the *most* and the *least* expensive antidepressant.
  - Effexor XR is viewed by a majority of PCPs as the most expensive antidepressant, followed by Paxil.
  - A majority view Celexa as the least expensive antidepressant, followed by an even split of responses between Paxil and Zoloft.
  - A majority of Psychiatrists also perceive Effexor XR to be the most expensive of these four products, followed by Zoloft.
  - Celexa is seen by a majority of Psychiatrists as the least expensive antidepressant, followed by Paxil.

Other Information Sources Regarding Antidepressant Availability and Price

- In addition to patients, who are the most influential and consistent source of cost and availability information for physicians, other sources of information include:
  - Pharmaceutical company representatives
  - Managed care organizations (formulary booklets/ cards)
  - Internet or PDA-based programs such as Eppocrates
  - Other on-line sources that convey information about local health plan' formularies.



Key Influencers That Shape Physicians Perceptions of Availability and Price
Cash-Payment and Co-Payment Patient Complaints

- While, in general, there is a perceived lack of hurdles to the availability and price of antidepressants, the most influential factors that shape physicians perceptions of availability and price, and, that in certain instances, can steer a physician to prescribe an alternative antidepressant are, in order of degree of influence:
  - #1: Cash-Paying Patient Complaints
  - #2: Co-Payment Patient Complaints
  - #3: Communication From Pharmacies Regarding Coverage Issues

Most Influential Elements That Shape Physicians Perceptions of Availability and Price
Cash-Payment Patient Complaints

- Complaints from the cash-paying patient are typically the most loudly voiced and most frequent complaints that shape physician' perceptions of availability and price.
  - This patient segment includes: Medicare and Medicaid recipients, the indigent, the working poor, the self-insured, and the affluent who have opted out of managed care.
  - Physicians will attempt to get approval for nonformulary medications for these patients, and if necessary, will seek alternative antidepressants, particularly for the less fortunate, indigent, and for Medicare patients on numerous medications who have a capped pharmacy benefit. However, physicians are very resistant to switching stabilized depressed patients.

Most Influential Elements That Shape Physicians Perceptions of Availability and Price
Co-Payment Patient Complaints

- Complaints from the co-payment patient are also frequent and strident.
  - This patient segment includes patients with HMO and PPO pharmacy benefit coverage.
  - These patients may complain that their co-payment amount has gone up, or, that the medication cost them more than what they have paid previously, or, that they paid more for this medication as compared to others drugs they take.
  - Physicians will attempt to get approval for nonformulary medications for these patients, and if necessary, will seek alternative antidepressants, though they may be less apt to jump through hurdles for chronic complainers who demonstrate an attitude of entitlement.

Most Influential Elements That Shape Physicians Perceptions of Availability and Price
Communication from Dispensing Pharmacies

- Communication from dispensing pharmacies, in the form of telephone calls and faxes, is the third most influence source of availability and price information.

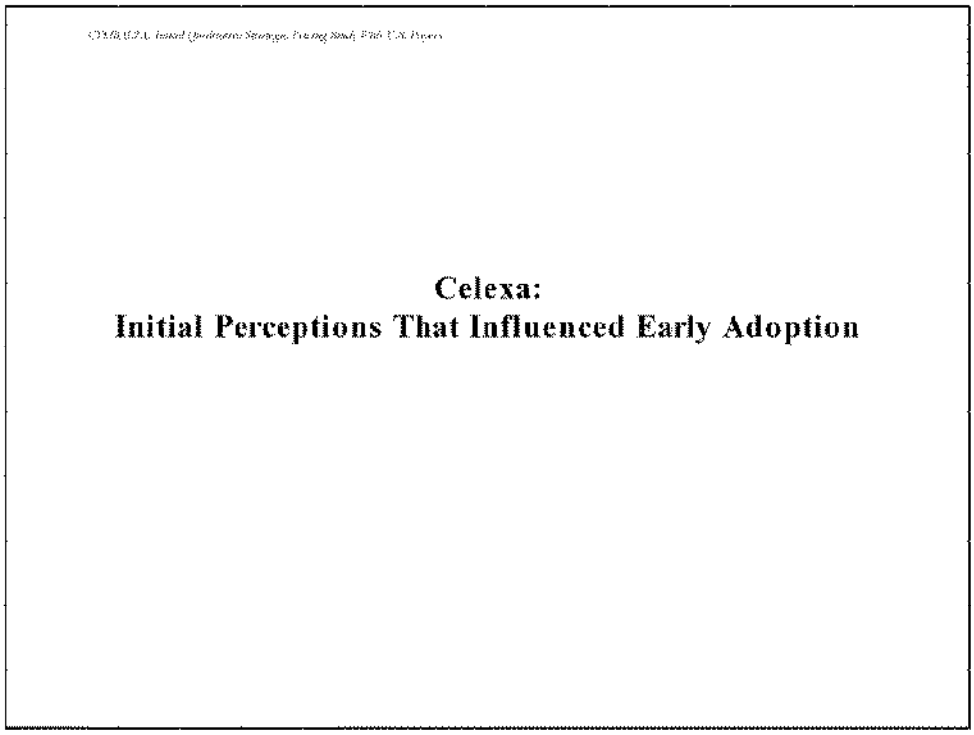
- This communication is often referred to by treating physicians as a daily bombardment or onslaught of requests:
  - Product is not on formulary, dosage strength is restricted
  - Product requires an appeals or approval process by the HMO
  - Product was on the patient's formulary last month, but is no longer a covered benefit
  - Patient's co-payment for this product has gone up and the patient requests an alternative.

Most Influential Elements That Shape Physicians Perceptions of Availability and Price
Communication from Dispensing Pharmacies

- Because physicians believe that antidepressants are widely available, communication from pharmacies is a less impactful hurdle and influencer of prescribing decisions for *this* therapeutic class, as compared to others, such as the PPIs, Statins, Antibiotics, and COX IIs.

Most Influential Elements That Shape Physicians Perceptions of Availability and Price
Other Potential Influencers

- Participants were asked about the degree to which other influencers pose a hurdle and their relative degree of impact on prescribing decisions.
- While all physicians receive communication directly from managed care organizations, in the form of letters, academic detailing, and occasionally, physician report cards, this information is not impacting physician prescribing decisions relative to antidepressants.
- Information from pharmaceutical representatives regarding the availability and price of their product or competitive products is also not perceived as influential.

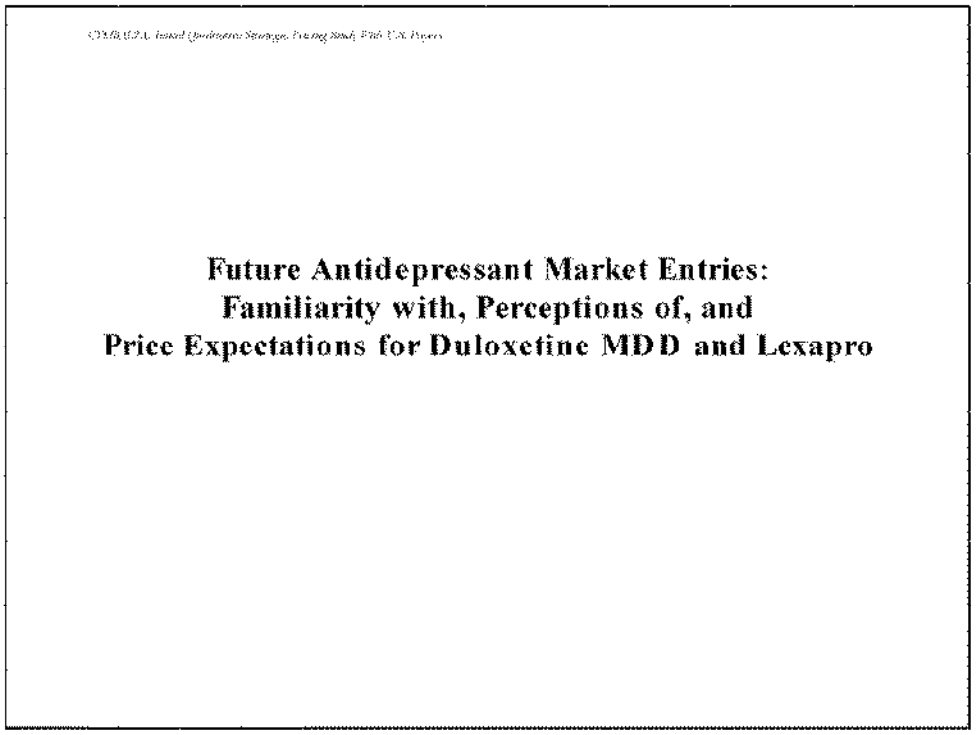


Celexa:
Early Adopters Swayed By Promotion Of Clinical Benefits

- Among Primary Care Physicians and Psychiatrists surveyed who were early adopters of Celexa, all shared a common trait of being highly influenced by Forest's positioning of clinical benefits relative to other SSRIs.
  - In particular, Forest's promotion of Celexa having fewer side effects was very compelling, specifically, *less sexual dysfunction, fewer drug-drug interactions*, and *better tolerated.*

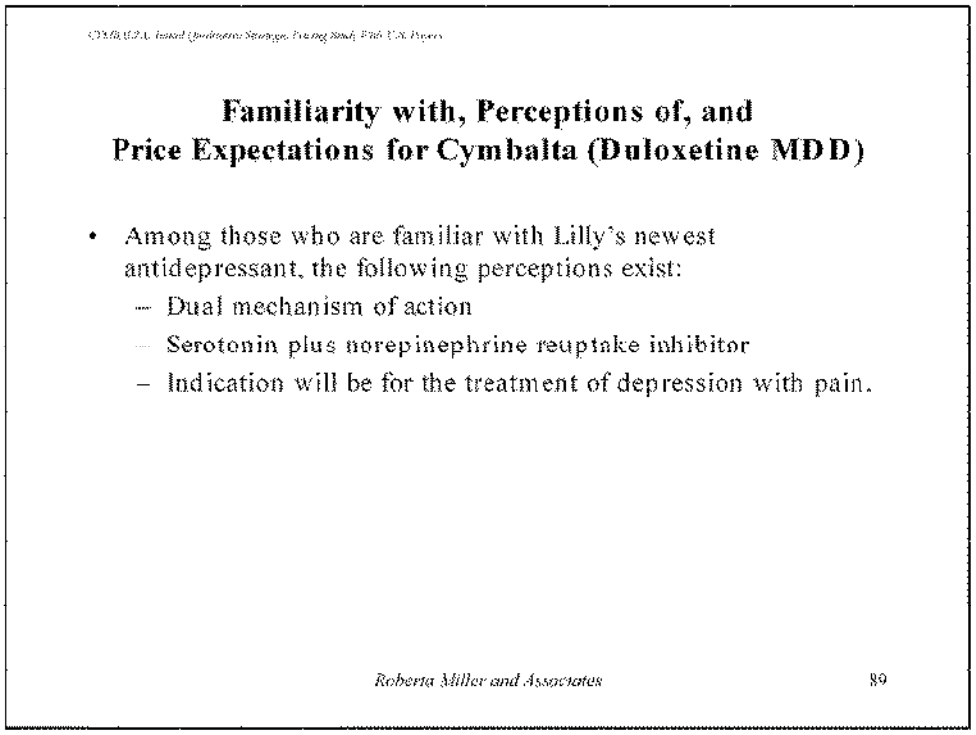
Celexa:
Early Adopters Swayed By Promotion Of Clinical Benefits

- Knowledge that Celexa was already marketed in Europe and that significant clinical data was available also influenced early adopters.
- While several recall Celexa being touted as cheaper and more cost effective, few physicians indicate that price influenced their early prescribing of the product.



Familiarity with, Perceptions of, and Price Expectations for Cymbalta (Duloxetine MDD)

- Less than half of all participants are familiar with Duloxetine MDD:
  - Fourteen (14) of Twenty-Four (24) Psychiatrists
  - Three (3) of Twenty-Three (23) Primary Care Physicians
  - Of the four markets surveyed, physicians in Atlanta and Chicago were the most familiar with Cymbalta; physicians from Philadelphia and Los Angeles the least familiar.



Familiarity with, Perceptions of, and Price Expectations for Cymbalta (Duloxetine MDD)

- Sources of information about Cymbalta have almost exclusively been different forums of communication from Lilly.
- Physicians hope, but do not necessarily expect, Cymbalta will come to market at a lower cost as compared to Effexor XR, in an effort to garner early acceptance and overall market share.
- A few physicians, Psychiatrists in particular, commented that they would expect a new antidepressant marketed by Eli Lilly to be expensive.
- A select few indicate they would expect the product to be expensive given its dual mode of action.

Familiarity with, Perceptions of, and Price Expectations for Cymbalta (Duloxetine MDD)

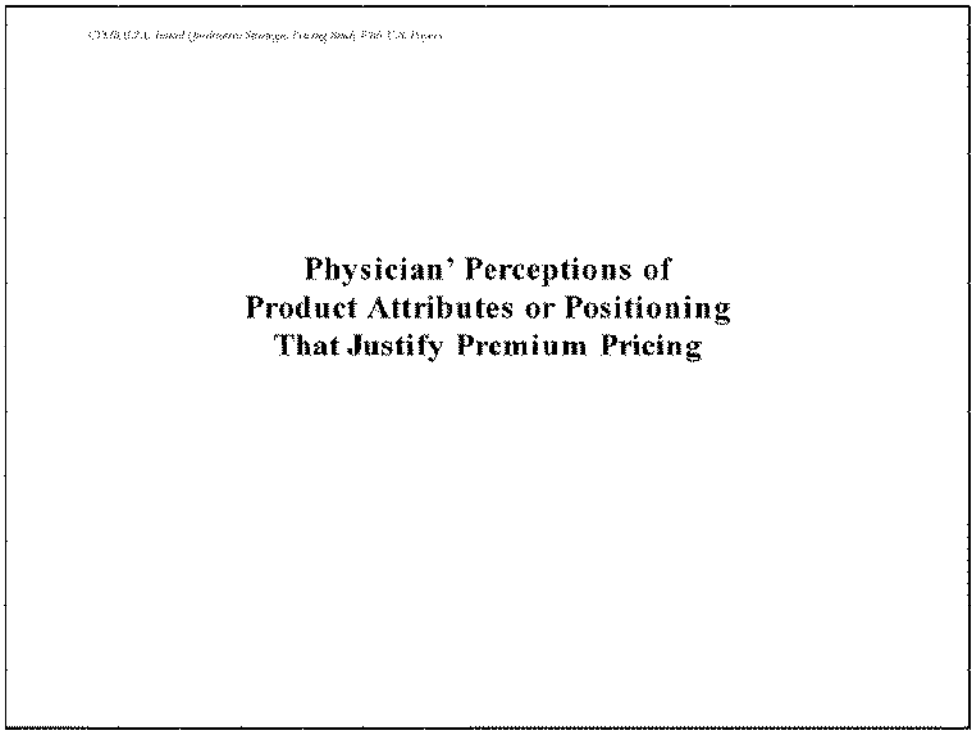
- Physicians are doubtful Cymbalta can compete at any price premium to Effexor XR.
- They believe that only three factors could justify or warrant consideration of premium pricing relative to Effexor XR:
  - Faster onset of action
  - Efficacy at a lower dose relative to Effexor XR coupled with Greater ease of titration, or,
  - A significant decrease in rate and severity of withdrawal/ discontinuation syndrome.

Familiarity with, Perceptions of, and Price Expectations for Lexapro

- A far greater number of physicians are familiar with Lexapro, as compared to Cymbalta.
- Greater than half of all participants are familiar with Lexapro:
  - Eighteen (18) of Twenty-Four (24) Psychiatrists
  - Eleven (11) of Twenty-Three (23) Primary Care Physicians
  - Of the four markets surveyed, physicians in Atlanta, Philadelphia, and Chicago were the most familiar with Lexapro; physicians from Los Angeles the least familiar.
- Information regarding Lexapro has come from Forest' representatives and clinical literature.

Familiarity with, Perceptions of, and Price Expectations for Lexapro

- Among those who are familiar with S-Citalopram, the following perceptions exist:
  - Isomer of Celexa
  - More potent/ efficacious
  - Improved side effect profile - a "cleaner" Celexa.
- Physicians believe Forest will enter the market with a similar pricing strategy as was undertaken for Celexa and that Lexapro will come to market at a lower cost to Celexa and all other SSRIs.
  - Improved efficacy, less sexual dysfunction, and lack of discontinuation syndrome could each, potentially, warrant premium pricing of Celexa.



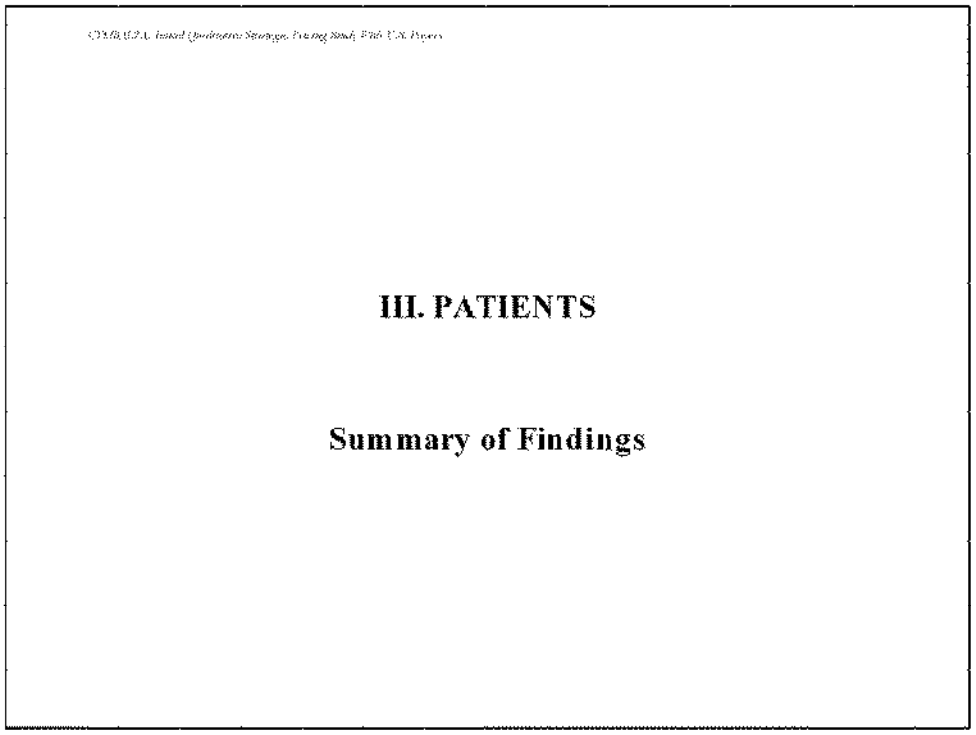
Physicians Draw No Inferences About the Clinical Value of a Pharmaceutical Products Based Upon Price (More Expensive versus Less Expensive)

- Physicians were asked if a product were introduced with a significant premium in price, relative to competitors, would they draw any inferences regarding the efficacy, safety, or clinical benefit of the product based upon its cost.

- All concur that they would not draw any inferences about the clinical value of a product based upon its price.

Product Attributes That Justify A Premium Price Over Other Antidepressants

- Improvement in efficacy, faster onset of action, and reduction in side effects relative to other antidepressants, are the key attributes that most quickly surface in physicians' minds as justification for premium pricing.
  - A reduction in sexual dysfunction is the most compelling side effect justification for premium pricing.
  - Minimization of withdrawal syndrome is also seen as important.



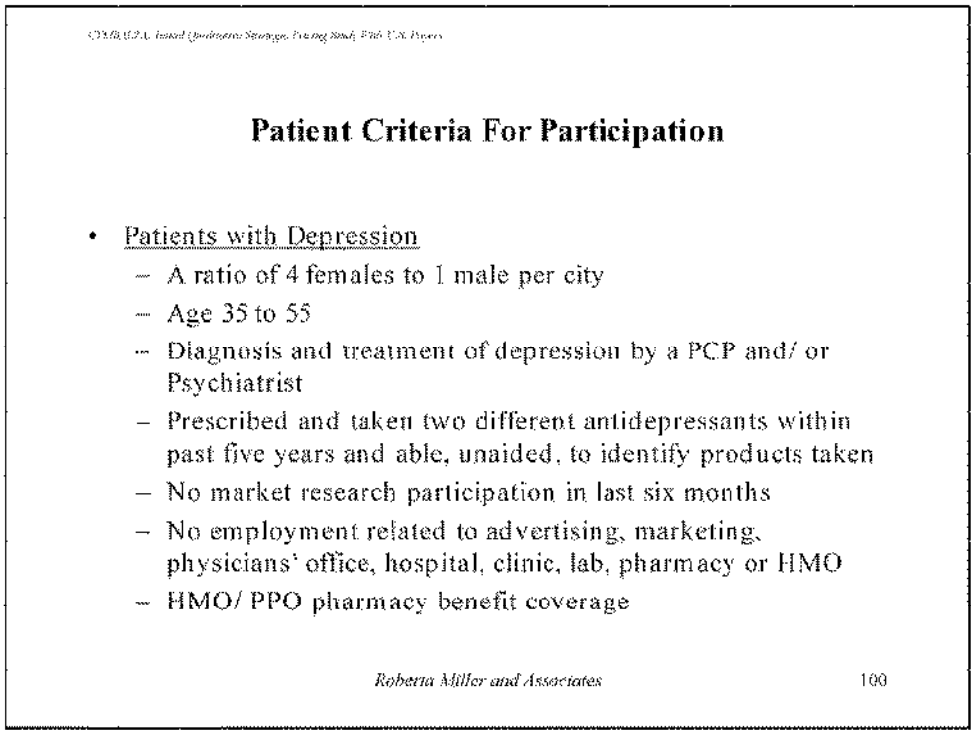
Patient Sample Demographics

- Patient research was fielded in the same four markets, during the same time frame, as the Physician research
- In-depth, one-on-one interviews were conducted with male and female patients in each of four markets (Atlanta, Philadelphia, Chicago, and Los Angeles)
- Patients surveyed have, collectively, taken most newer antidepressants in the past five years:
  - Prozac, Prozac Weekly, Paxil, Zoloft, Celexa, Wellbutrin, and Effexor
  - Each participant has taken at least two antidepressants in the past five years.

Patient Sample Demographics

- Total Patient Representation N=22
  - Atlanta N=4
    - 4 Females
  - Philadelphia N=7
    - 6 Females
    - 1 Male
  - Chicago N=6
    - 5 Females
    - 1 Male
  - Los Angeles N=5
    - 4 Females
    - 1 Male

Roberta Miller and Associates 99



A Note About Participant Patients

- For those who did not view the research live, it is important to put in to context the experience of depression among patients surveyed.
- All of the patients from this study exemplify how difficult it is to determine the "ideal" antidepressant for a given individual (optimal efficacy, coupled with minimal, tolerable side effects.)
- They also exemplify patients suffering from depression who are truly treatment seekers. Each continued to seek care, by visiting multiple physicians and trying multiple pharmaceutical products, in an effort to achieve healthier and more meaningful and productive lives.

The Context In Which Patients View Cost and Out-of-Pocket Expense

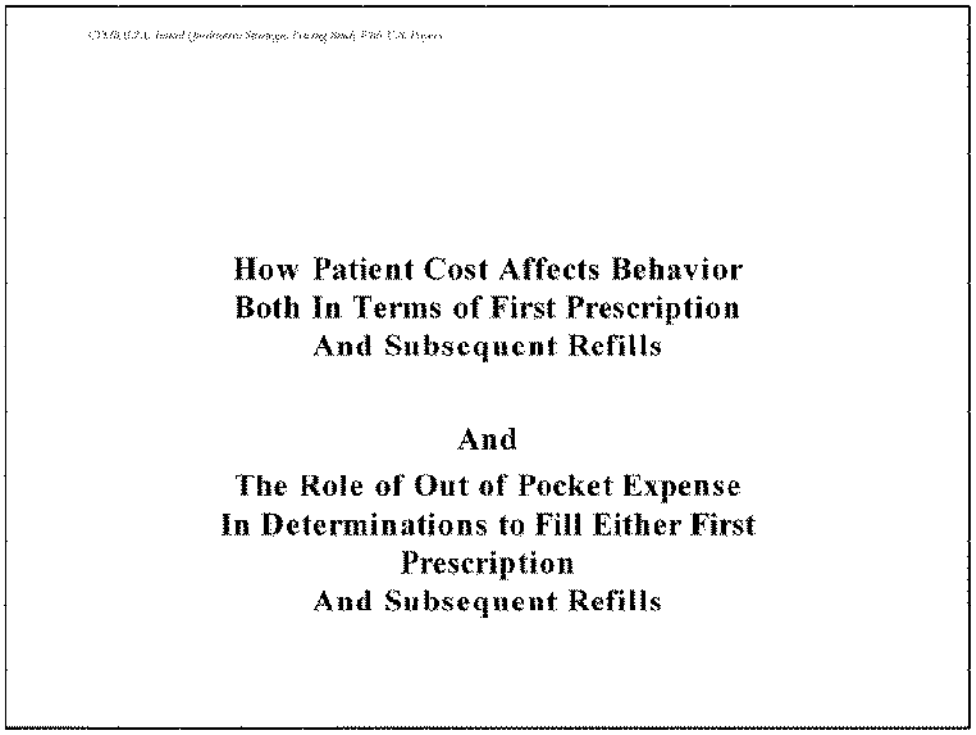
Absolute Dollars

Versus

Incremental Dollars Over Alternatives

The Context In Which Patients View Cost and Out-of-Pocket Expense *Absolute Dollars*

- Patients with managed care coverage and a pharmacy benefit think about cost and out of pocket expense in terms of absolute dollars they pay for a medication in the form of a co-payment.
- Patients with a pharmacy benefit do not typically think about the cost of a medication - positively or negatively, particularly a chronic medication, which they view as essential to their health and well being, such as an antidepressant.
- Patients who take multiple medications for complex conditions an/ or co-morbidities think of cost in terms of *total, cumulative* absolute out of pocket dollars incurred on a monthly basis.



How Patient Cost Affects Behavior Both In Terms of First Prescription And Subsequent Refills

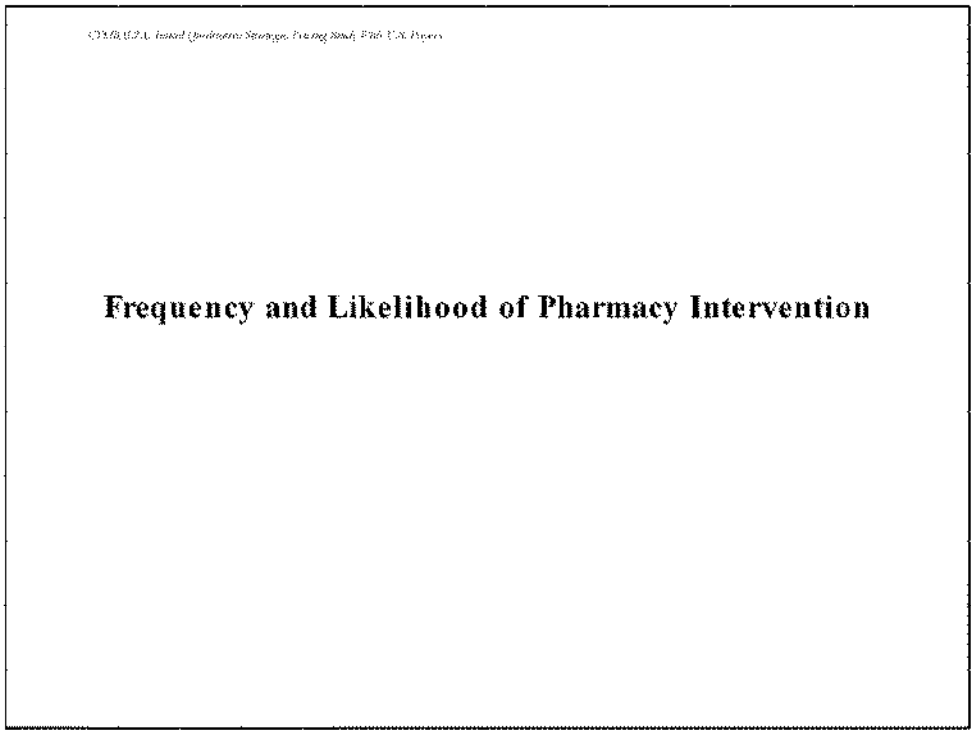
- All patients surveyed place great importance on their mental well being and its impact on their functionality and quality of life.
- As a result, patients are far more likely to fill both a first prescription and subsequent refills of an antidepressant they view as effective and relatively well-tolerated.

The Role of Out of Pocket Expense In Determinations to Fill Either First Prescription And Subsequent Refills

- Patients may delay the purchase of an initial prescription, or not fill it altogether, if the out of pocket cost is significantly greater than a typical co-payment and, if they view the product as non-essential or something they can do without.
- Among all patients surveyed, an effective antidepressant is viewed as an essential, a necessity.
- Patients will pay for any **antidepressant** they feel is providing a beneficial outcome - even if their co-payment for the product increased by twenty dollars per prescription (a typical differential between a two tier and a three tier co-payment.)

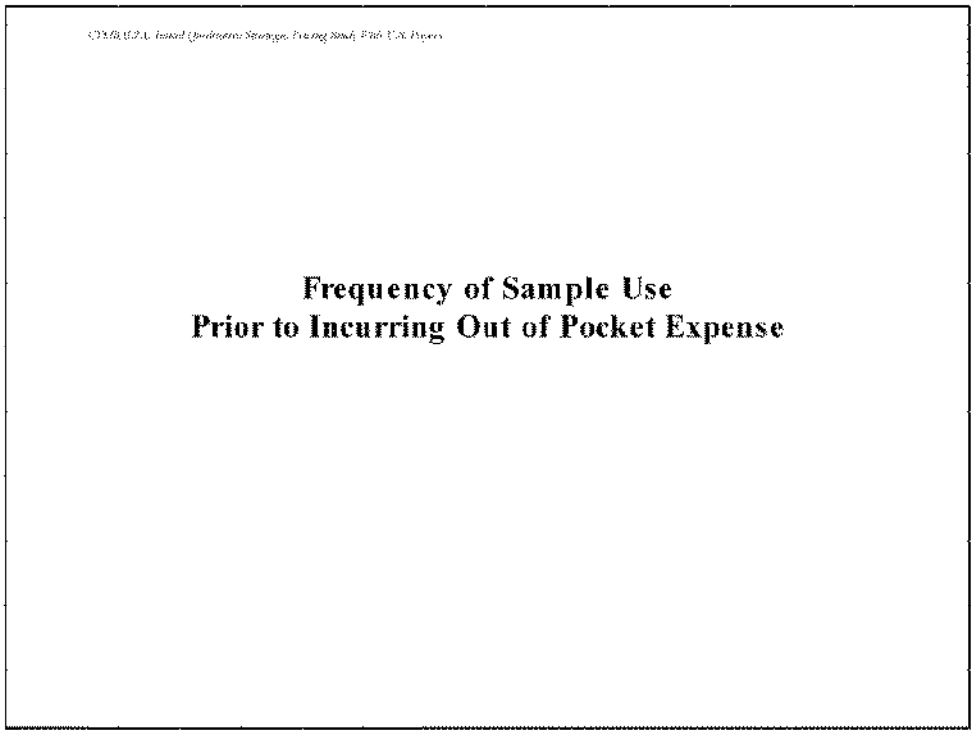
How Patient Cost Affects Behavior Both In Terms of First Prescription And Subsequent Refills

- Products for which an initial prescription and subsequent refills may not be filled because of cost, i.e., out of poeket expense - or where the patient might ask for a generic or lower cost alternative include:
  - Products taken on a PRN basis:
    - Migraine treatments, such as Imitrex
    - Topical Antifungals, such as Lamisil
    - Antivirals, such as Zovirax for Herpes
  - "Lifestyle" products:
    - Renova for mitigation of wrinkles
  - Acute treatments that are nonformulary or cost significantly more in terms of out of pocket expense than normally incurred
    - Antibiotics
    - Antihistamines



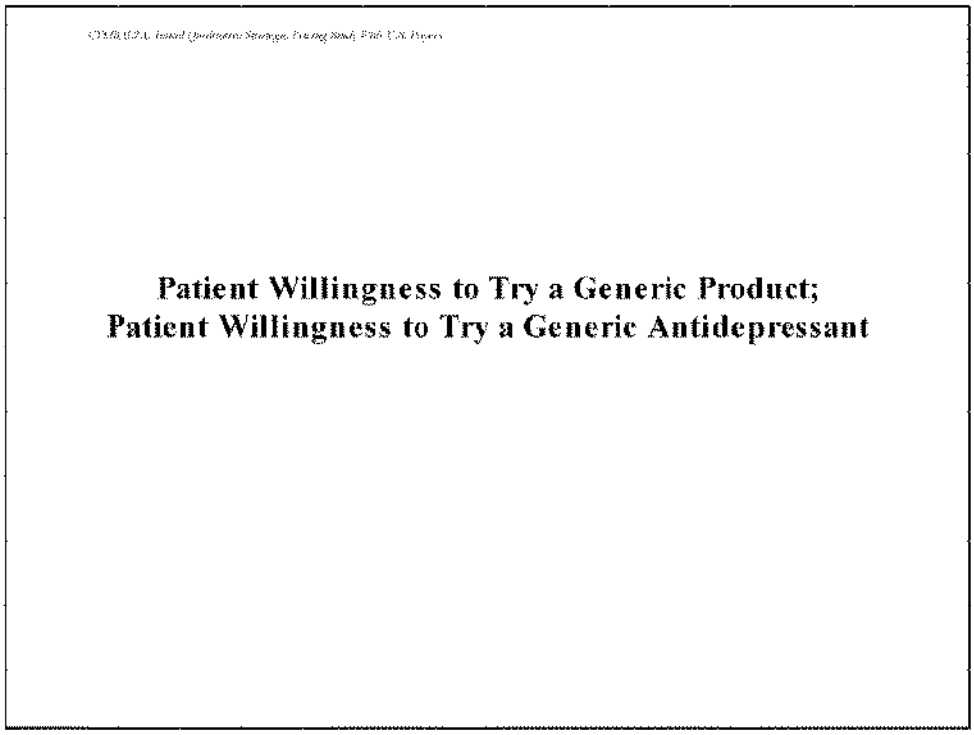
Frequency and Likelihood of Pharmacy Intervention
Fairly Frequent and Routine

- Most patients surveyed are routinely informed by a pharmacist or pharmacy technician when a lower cost alternative to the medication their physician prescribed is available.
- Patient response varies based upon their view of a specific medication and therapeutic class. Again, for patients who are stabilized on an antidepressant, particularly among patients that have tried two or more products, there is far less willingness to be switched to a lower cost brand or generic alternative.
- Patients frequently want to speak with their physician prior to accepting a cheaper alternative to the medication prescribed.



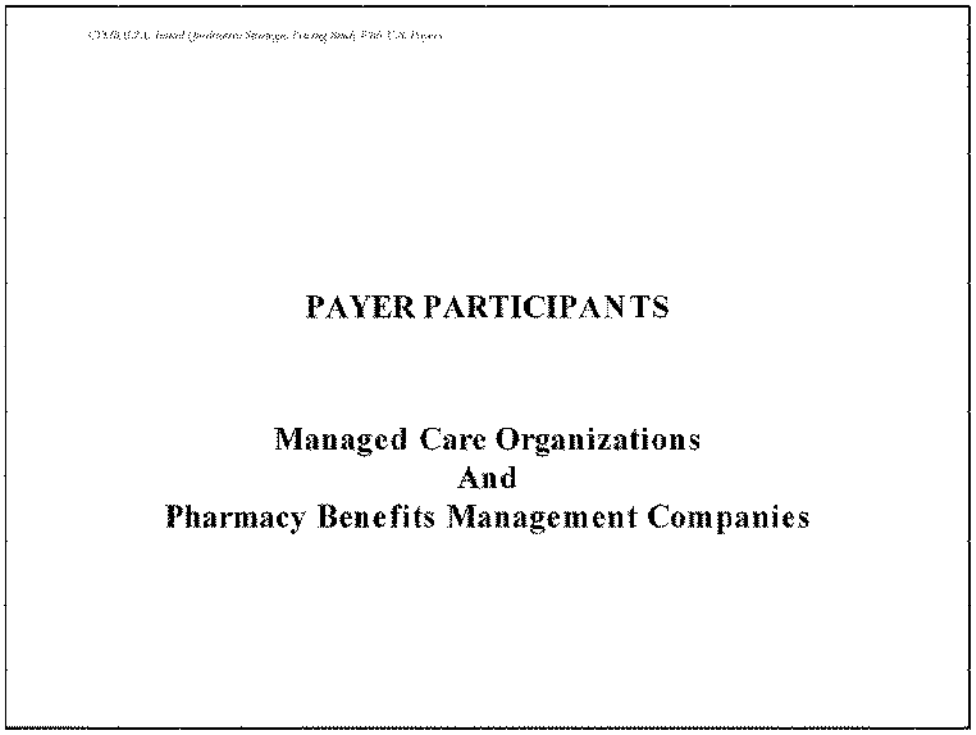
Frequency of Sample Use
Prior to Incurring Out of Pocket Expense
Frequent and Routine

- The majority of patients surveyed routinely receive samples prior to having to pay out of pocket when initially starting a medication.
- Most received samples of first and subsequent antidepressants prescribed for them, and a few patients continue to receive samples, periodically, as part of their ongoing treatment for depression.



Patients Are Open to Trying A Generic Product But Would Not Switch If Stabilized On An Antidepressant

- Patients are willing to try a generic product and have frequently tried generic products in other therapeutic classes.
- However, patients who are stabilized on an antidepressant are not willing to be switched, at the pharmacy, to a generic **antidepressant**.



Participating Organizations

- *Altius Health Plans, UT*
- *AV-Med Health Plan, FL*
- *Blue Care Network, MI*
- *Blue Cross/Blue Shield of Kentucky, KY*
- *Blue Cross of California, CA*
- *CHA Health, KY*
- *Cigna Health Care, TX*
- *Coventry Health Care, TN*
- *Dean Health Plan, WI*

Participating Organizations

- *Excellus Blue Cross/Blue Shield, NY*
- *Group Health Cooperative of South Wisconsin, WI*
- *Henry Ford Medical Group, MI*
- *Intermountain Health Care, UT*
- *Kaiser Permanente, CA*
- *Medica, MN*
- *Med Impact, IN [PBM]*
- *Mid Atlantic Medical Services, Inc., MD*
- *Ochsner Health Plan, LA*

Participating Organizations

- *Oxford Health Plan, CT*
- *PacifiCare, CA [Rx Solutions - PBM]*
- *Penn State Geisinger Health Systems, PA*
- *Premera Blue Cross, WA*
- *United Health Care of Wisconsin, WI*